Humic Acids (HA) Strongly Potentiate Anti-HIV Effects of AZT, Griffithsin, and Cyanovirin

Article *in* AIDS Research and Human Retroviruses · October 2014

DOI: 10.1089/aid.2014.5441.abstract · Source: PubMed

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Results: There are at least six key ethical considerations for Canadian stakeholders to consider in the fair selection of subjects for HVTs: duty to include; duty to exclude; respect for communities; risk-benefit profile and net risk; public health research; and global distributive justice.
Conclusions: This exploration encourages an ethical analysis of fair subject selection that accounts for both domestic and global responsibilities, and that uses a ''reflective equilibrium'' approach. More debate, discussion and commentary among HVT stakeholders in Canada is necessary to ensure that key moral tensions have been described, addressed and, where possible, consensus reached.

P32.03
HIV and the Law: The Impact of the Law on HIV Research and the Role of Researchers

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Background: There is a growing need to fully explore the connection between the law and HIV, and the negative impact the law can have. Internationally, there is an alarming growth in the popularity of anti-gay laws, which are likely to have a significant impact on the spread of HIV. While the myth that HIV is a disease that plagues homosexuals alone has long been proven false, nevertheless, men having sex with men (MSMs) are a high risk population that suffers from stigma and discrimination that often results in them avoiding the health care system or not receiving the treatment they need. These laws only stand to exacerbate this problem. Furthermore, the stereotype that a man who has contracted HIV is gay has unfortunately not been completely eliminated. As such, these laws may cause heterosexual, as well as homosexual, HIV-positive men to avoid the health care system, fearing criminalization and prejudice. In addition to anti-gay laws, there are HIV criminalization statutes that still not been eliminated, with recent legal cases exhibiting the impact that the legal system can have on public health, and the HIV epidemic specifically. The purpose of this presentation is to analyze and educate how these laws and the enforcement and interpretation of them can impact the HIV community and, in fact, hinder the goal of slowing the spread of the disease. By increasing stigma and misconceptions, while reducing education and understanding, the effect of criminalization laws needs to be fully explored and understood to aid in their eventual elimination. Moreover, there is a growing need to explore the roles of researchers and potential obligations they may have in relation to participants and the legal threats they face.

Evaluation of Novel Compounds in Cell-Based Systems

P33.01
HIV-1 Shows Increased Sensitivity to Griffithsin Derivatives

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Background: The lectin griffithsin (GRFT) is a homodimer isolated from the red alga griffithsia sp. GRFT has demonstrated potent and broad anti-HIV-1 activity across subtypes and is one of the leading HIV-1 microbicide candidates. The GRFT Derivatives 2MG, 2MG3, 3MG and 4MG are made of arrays of two, three and four monomeric GRFT units, respectively.
Methods: We evaluated HIV-1 subtype A, B and C against 2MG, 2MG3, 3MG, 4MG and GRFT using the TZM-bl neutralization assay. GRFT derivatives were also tested for their inhibition of the cell-to-cell transmission of HIV-1. The 234 and 295 glycans, shown to be important in GRFT binding to HIV-1, were introduced in the virus by site directed mutagenesis, and their effects on 2MG, 2MG3, 3MG and 4MG binding studied. GRFT resistant viruses were generated by culturing HIV-1 under escalating concentrations of the lectin. These resistant viruses were then tested for sensitivity to 2MG, 2MG3, 3MG and 4MG.
Results: In general 2MG and 2MG3 were as potent as GRFT against all the viruses tested while 3MG and 4MG were more potent against HIV-1 subtype A and C. GRFT was also less potent than these two derivatives in the inhibition of cell-to-cell transmission of HIV-1. Similar to GRFT, the introduction of the 234 and 295 glycans affected HIV-1 sensitivity to 2MG and 2MG3; while it did not affect 3MG and 4MG neutralization of the virus. Lastly, GRFT resistant viruses showed sensitive to 3MG and 4MG.
Conclusions: The 3MG and 4MG derivatives were more potent than GRFT in inhibiting HIV-1 infection. Also viruses that showed resistance to GRFT remained sensitive to these compounds. It is possible that 3MG and 4MG binding site on the viral envelope is different from that of GRFT given that the 234 and 295 glycans do affect their neutralization of the virus. The data generated from these studies suggests that linking GRFT into arrays of more than two monomeric units increases its potency against HIV-1.

P33.02
Antiviral Activity and Mode of Action of Griffithsin against HSV-2 and HPV: Preliminary Studies of a Potential non-ARV Combination Microbicide

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Background: Griffithsin (GRFT) is a promising HIV microbicide candidate. Nixon et al. have shown that GRFT blocks herpes simplex 2 (HSV-2) infection in a mouse model, proposing inhibition of cell-to-cell spread as the mode of action (MOA). Using *in vitro* studies we further investigated the MOA of GRFT against HSV-2 and studied its antiviral activity against human papillomavirus (HPV). We also combined GRFT with zinc acetate (ZA) and/or carrageenan (CG) to render a more potent microbicide.