Flexible, Polyvalent Antiviral Dendritic Conjugates for the Treatment of HIV/AIDS

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Technology description

Summary

This technology describes the design and synthesis of flexible, polyvalent, antiviral conjugates of less than 200 kDa for the treatment HIV/AIDS. These conjugates are mimetic of D1D2-Igatp, a high-molecular-weight (1 MDa) CD4-immunoglobulin fusion construct with extreme HIV neutralizing potency. Cryo electron microscopy suggests that the extreme potency of D1D2-Igatp is due to polyvalent presentation of a gp120-binding ligand on a flexible scaffold. The current prototype for the technology is a conjugate comprising soluble, two-domain human CD4 covalently linked to a flexible poly(ethylene glycol)-PAMAM dendrimer scaffold. The construct is designed to retain a high degree of flexibility and polyvalence, and, at less than 200 kDa, is similar in size to successful antibody therapeutics currently on the market. Because it retains the key determinants of potency and the human CD4 moieties of D1D2-Igatp, this conjugate is expected to have the following unique set of HIV antiviral properties: (1) IC_{90} infectivity neutralization values in the nanomolar range against HIV primary isolates; (2) lack of susceptibility to viable escape mutations, because the ligand is CD4, and because CD4-independence evolves concomitantly with constitutive exposure of neutralization-sensitive, highly conserved coreceptor binding site epitopes; (3) indefinite control of HIV viral replication, without the need for combination therapy, arising from properties (1) and (2); (4) improved HIV viral replication control when used in combination with other Highly Active Antiretroviral Therapy (HAART); (5) improved prevention of seroconversion when used in combination with other HAART shortly following known exposure to HIV.

Application area

Novel therapeutics for the treatment and prevention of HIV infection

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com