

**HIV-1/SIV Chimeras Promoting Trimerization of Soluble HIV-1 ENV**

Bernard Moss (NIAID). U.S. Provisional Application filed 10 Oct 2003 (DHHS Reference No. E-356-2003/0-US-01). *Licensing Contact:* Susan Ano; (301) 435-5515; [anos@mail.nih.gov](mailto:anos@mail.nih.gov).

The technology describes the replacement of the gp41 segment of HIV-1 gp140 or just the N-terminal portion (85 amino acids) with the corresponding region of SIV to promote efficient trimerization. Functional, virion associated HIV-1 and SIV env have been shown to have an almost exclusively trimeric structure. The chimera that contains only the N-terminal portion of SIV in an HIV-1 background is particularly interesting, since several broadly neutralizing HIV-1 epitopes are present in the C-terminal segment of gp41. Thus, the current technology could be useful as an immunogen to elicit antibodies that recognize a mimic of the native trimeric structure. The region of HIV-1 replaced by SIV sequence contains no known targets of neutralizing antibodies.

**Use of a Statin To Kill EBV-Transformed B Cells**

Jeffrey Cohen *et al.* (NIAID). U.S. Provisional Application filed 28 Oct 2003 (DHHS Reference No. E-312-2003/0-US-01).

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This technology describes the use of certain natural and synthetic statins, including simvastatin, other leukocyte function antigen-1 (LFA-1) inhibiting statins, and compounds derived from LFA-1 inhibiting statins and statin-like compounds, for treatment or prevention of Epstein-Barr Virus (EBV) associated tumors, including lymphomas that express LFA-1 and transforming proteins. Such compounds could also be used to treat tumors associated with other viruses that express LFA-1. Cancers associated with EBV that could be treated with the statins by methods described herein include nasopharyngeal carcinoma, Hodgkin's disease, lymphoproliferative disease, T-cell lymphoma, and non-Hodgkin's lymphoma.

**HIV-Dependent Expression Vector**

Drs. Jon Marsh and Yuntao Wu (NIMH). U.S. Provisional Application No. 60/507,034 filed 28 Sep 2003 (DHHS Reference No. E-276-2003/0-US-01).

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This invention provides a DNA construct that can be useful for both

diagnostics and AIDS therapeutics. The construct can be incorporated into a retrovirus or into a cell line. This construct mediates the expression of a selected gene in the presence of HIV replication, but is silent in the absence of HIV. The cell line with the incorporated construct can be used as an indicator line for the presence of replication-competent HIV. The virus containing the construct can be used to co-infect a population of HIV-infected cells. If the construct-encoded gene is a reporter, it would specifically identify cells that are infected with HIV. If the construct-encoded gene is a cytotoxin, it would specifically kill cells that are HIV-infected. This invention may offer a novel approach to HIV elimination, as well as detection of HIV infected cells or the presence of cell-free infectious HIV.

**Polypeptide Multimers Having Antiviral Activity**

Carol Weiss *et al.* (FDA). PCT Application filed 14 Aug 2003 (DHHS Reference No. E-155-2003/0-PCT-01); U.S. Patent Application No. 09/480,336 filed 07 Jan 2000 (DHHS Reference No. E-212-2001/0-US-02).

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The technology describes polypeptide multimers that have antiviral and immunogenic activity against HIV. These multimers consist of at least one monomer of the highly conserved N and C heptad regions of gp41 in a ratio of at least 2:1 N to C heptad, with the N and C heptads being connected by linkers. The monomer forms homodimers and homotrimers in solution and mimic fusion intermediate structure. Further, the technology also describes a method of raising a broadly neutralizing antibody response to HIV by administering the polypeptide multimers mentioned above. Thus, these polypeptide multimers may be used as antiviral (anti-HIV) agents. Because the structure of these polypeptide multimers mimics the gp41 fusion intermediate, they can also be used to identify compounds that may inhibit the fusion process.

**Discovery of Novel Inhibitors of HIV-1 Integrase and/or RNase H That Can Be Used for the Treatment of Retroviral Infection Including AIDS**

Stuart F. J. Le Grice (NCI) *et al.* U.S. Provisional Application filed 31 Oct 2003 (DHHS Reference No. E-022-2003/0-US-01).

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This invention provides compounds and methods of treating retroviral

infection such as AIDS by administration of a dioxotetrahydrobenzo[a]naphthacene compound, particularly a 8,13-dioxo-5,6,8,13-tetrahydrobenzo[a]naphthacene compound, *i.e.* a madurahydroxylactone compound. Retroviruses, such as HIV, need three viral enzymes for replication: reverse transcriptase, protease, and integrase. The prognosis of AIDS patients has recently been improved by the discovery and associated therapeutic administration of reverse transcriptase and/or protease inhibitors. However, a significant portion of AIDS patients fail to respond to such treatments and viral resistance remains a major problem.

It is known that HIV-1 integrase is a rational target for AIDS therapy because genetic studies have demonstrated that the enzyme is essential for viral replication, and because there is no cellular equivalent. On the other hand, the reverse transcriptase RNase H active site is another good target for antiviral therapeutic development because elimination of the RNase H activity of reverse transcriptase arrests virus replication. The compounds reported in this invention may be capable of inhibiting both enzymes since the catalytic centers of integrase and RNase H are structurally similar. As a consequence, this invention can potentially avoid viral resistance, which limits the efficacy of presently administered reverse transcriptase and/or protease inhibitor therapeutic agents. Thus, the invention may be a group of new small molecule agents for treating patients suffering from retroviral infections, particularly patients suffering from Human Immunodeficiency Virus (HIV).

**Particles for Imaging Cells**

Kathleen Hinds, Cynthia Dunbar (NHLBI). U.S. Patent Application No. 10/313,304 filed 06 Dec 2002 (DHHS Reference No. E-185-2002/0-US-01).

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Available for licensing are NIH patent pending contrast particles for use in MRI and flow cytometry to track cells migration in real time. Present cell-tracking studies rely on labeling cells with ultra-small dextran-coated iron particles that are endocytosed. The contrast agent of the present invention uses larger iron oxide particles, approximately 1  $\mu\text{m}$ , situated in a tri-layer structure. The inner structure is a magnetic molecular complex of FITC (a fluorescent marker) encased in a layer of superparamagnetic microparticles, which is then covered with a shell of