This invention relates to methods and compositions for the attenuation of HIV–1 replication in human cells, and especially in human macrophages by targeting a host cell protein. HIV–1 infected macrophages typically resist cell death, support viral replication, and facilitate HIV–1 transmission. We found that the gene encoding cyclin-dependent kinase inhibitor 1A (CDKN1A) is consistently expressed following virus binding, and re-expressed at the peak of HIV–1 replication. The protein encoded by this gene, also known as p21, is associated with cell cycle regulation, anti-apoptotic response and cell differentiation. Increased levels of p21 may enhance survival and long-term persistence of HIV–1 infected macrophages. Treatment of cultured infected cells with antisense p21 oligonucleotides or p21 short interfering RNA (p21 siRNA) significantly reduced replication of HIV–1. A similar effect was observed when infected cells were exposed to the synthetic triterpenoid CDDO, a potent multifunctional agent that influences differentiation and has anti-inflammatory and anti-proliferative properties, including inhibition of p21. Neither p21 oligonucleotides nor CDDO were toxic to the cultured macrophages. Thus, p21 inhibitors could be safe and effective anti-HIV therapeutic candidates to be used in conjunction with current anti-retroviral therapy.

Cannula for Pressure Mediated Drug Delivery

Stephen Wiener, Robert Hoyt, John Deleonardis, Randal Clevenger, Robert Lutz, Brian Safer (NHLBI).

PCT Application No. PCT/US99/11277 filed 21 May 1999, which published as WO 99/59666 on 25 Nov 1999 (DHHS Reference No. E–196–1998/2–PCT–01); U.S., Australian, Japanese, and European rights pending.

Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov*.

Available for licensing are methods and devices for selectively delivering therapeutic substances to specific histological or microanatomical areas of organs (*e.g.*, introduction of the therapeutic substance into a hollow organ space such as the hepatobiliary duct or the gallbladder lumen) at a controlled pressure, volume and/or rate which allows the substance to reach a predetermined cellular layer. The volume or flow rate of the substance can be controlled so that the intralumenal pressure reaches a predetermined threshold beyond which subsequent subepithehal delivery of the substance occurs. Alternatively, a lower pressure is selected that does not exceed the threshold level, so that delivery occurs substantially to the epithelial layer. Such site-specific delivery of therapeutic agents permits localized delivery in concentrations that may otherwise produce systemic toxicity. Occlusion of venous or lymphatic drainage from the organ can also help prevent systemic administration of therapeutic substances, and increases selective delivery to superficial epithelial cellular layers. Delivery of genetic vectors can also be delivered to target cells. The access device comprises a cannula with a wall piercing tracar within the lumen. Two axially spaced inflatable balloons engage the wall securing the cannula and sealing the puncture site. A catheter equipped with an occlusion balloon is guided through the cannula to the location where the therapeutic substance is to be delivered.

Dated: April 22, 2004.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 04–9685 Filed 4–28–04; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Institute Review Group, Subcommittee G—Education.

Date: June 16–18, 2004

Time: 8 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Sheraton Suites Alexandria, 801 North Saint Asaph Street, Alexandria, VA 22314.

Contact Person: Ilda M. Mckenna, Scientific Review Administrator, Research Training Review Branch, Division of Extramural Activities, National Cancer Institute, 6116 Executive Boulevard Room 8111, Bethesda, MD 20892, (301) 496–7481, *mckennai@mail.nih.gov*.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: April 21, 2004.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 04–9682 Filed 4–28–04; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Institute Initial Review Group; Subcommittee F—Manpower & Training.

Date: June 14–15, 2004.

Time: 8:30 a.m. to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn Georgetown, 2101 Wisconsin Avenue, NW., Washington, DC 20007.

Contact Person: Lynn M. Amende, PhD, Scientific Review Administrator, Resources and Training Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard Room 8105, Bethesda, MD 20892, 301–451–4759, *amendel@mail.nih.gov*.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology