the fields of Magnetic Resonance Imaging, Magnetic Resonance Spectroscopy, Molecular Imaging, Image Processing, and Surgery Under Image Guidance. Particular emphasis is placed on discoveries that enhance clinical research.

Under a CRADA, the NIHCC can offer selected collaborators access to facilities, staff, materials, and expertise. The collaborator may contribute facilities, staff, materials, expertise and funding to the collaboration. The NIHCC cannot contribute funding. The CRADA collaborator may elect an option to an exclusive or non-exclusive license to Government intellectual property rights arising under the CRADA and may qualify as a co-inventor of new technology developed under the CRADA.

CRADA proposals will be evaluated under the following criteria:

- Corporate research and development competencies.
- Demonstrated abilities to productively collaborate in research programs.
- The nature of resources to be contributed to the collaboration.
- Key staff expertise, qualifications and relevant experience.
- Willingness to assign technical staff to on-site collaborative efforts.
- Ability to effectively commercialize new discoveries.

Dated: August 26, 1998.

Kathleen Sybert,

Acting Director, Technology Development and Commercialization Branch, National Institutes of Health.

[FR Doc. 98–24370 Filed 9–10–98; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7057; fax: 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

LIF And Related Cytokines That Operate Through The gp130 Receptor Pathway As A Means To Enhancing Embryo Implantation In Mammals And As An Alternative To Using Estrogen

CL Stewart, T Shatzer, T Sullivan, JR Chen, L Hernandez (NCI)

DDHS Reference No. E–166–98/0 filed 06 Jul 98

Licensing Contact: Dennis Penn, 301/496–7056 ext. 211

The present invention is directed to the use of Leukemia Inhibitory Factor (LIF), or certain other cytokines as a means for enhancing successful embryo implantation. This discovery may lead to increased success rates in normal embryonic development in human and non-human embryos following in vitro fertilization. The present invention, tested in LIF deficient mice, confirms that single injections of LIF lead to implantation and the embryo's normal development to birth. LIF may be useful as a replacement for estrogen in inducing embryo implantation. The invention indicates that LIF can substitute for estrogen in animal models, in regulating the receptibility of the uterus to the implanting embryo, and results in a significant increase in successful implantation. This technology has both human and veterinary applications.

Protection Of Neural Cells From Catecholamine-Induced Apoptosis By Macrophage Migration Inhibitory Factor (MIF)

G Wistow (NEI)

DDHS Reference No. E–028–98/0 filed 28 Jul 98

Licensing Contact: Stephen Finley, 301/496–7735 ext. 215

Macrophage Migration Inhibitory Factor (MIF) was shown to have neuroprotective properties with important implications for conditions such as Parkinson's Disease (PD). MIF is widely distributed in mammalian tissues. However, in vivo studies show that while the levels of MIF expression significantly decrease with age in most tissues, including lens, liver and kidney, it is maintained at high levels in neural tissues, brain and retina. This suggests the possibility of an important role for MIF in aging neural tissues. It was also shown that MIF has catalytic enzyme activity towards the toxic quinonesdopaminechrome (DNC), epinephrinechrome (EC) and noreprinephrine (NEC) which arises by oxidation of the catecholamine neurotransmitters dopamine, epinephrine and norepinephrine. These catecholamines induce cell death by apoptosis in cultured neural cells and other cell types. It was shown that in cell culture, MIF can block this catecholamine-induced cell death. Death of catecholaminergic neurons is an important feature of PD in human brain. This suggests a physiological and/or therapeutic role for MIF in protection of neural and other cells from apoptosis induced by toxic quinones. Decreased levels of MIF in the aging brain may be a risk factor for PD and similar neurodegenerative disorders. MIF may also be involved in the synthesis of neuromelanin, which is prominent in the aging human substantia nigra, since the guinones DNC, EC and NEC are known neuromelanin precursors.

A surprising additional property of MIF was also observed. Lens epithelial cell cultures differentiated into neuronlike cells, containing neuronal cell markers, axons, and processes, upon the constitutive expression of endogenous recombinant MIF. Thus, in addition to its neuroprotective properties, MIF has potential to contribute to culture methods for neural cells that may be useful in transplantation.

G-Protein Coupled Receptor Antagonists

N Tarasova, SJ Michejda (NCI)

Serial No. 60/076,105 filed 27 Feb 98

Licensing Contact: Carol Salata, 301/496–7735 ext. 232

This invention is a potentially broadly applicable method of disrupting the functioning of G-protein coupled receptors (GPCR). GPCRs are a large familly of receptors involved in the regulation of physiological activities. GPCRs have seven transmembrane regions, i.e. they cross the cell membrane seven times. The inventors have found that if a peptide consisting of one of the transmembrane regions of a GPCR with an added charged amino acid on the extracellular side, is brought into contact with a cell having the same GPCR, the functioning of the GPCR is disrupted. It is thought that the added peptide interferes with the correct assembly of the GPCR. Cells containing

the CXCR4 receptor, a co-receptor with CD4 for the entry of certain strains of HIV-1 into T-cells, are much less receptive to infection by HIV in the presence of a particular transmembrane peptide from the CXCR4 receptor. Therefore, this method of disrupting the functioning of particular GPCRs could be used to treat diseases which are mediated by functioning GPCRs, such as HIV.

Inhibition of HFG/SF Cleavage/ Activation by Suramin and Other Related Small Molecules

C Webb, ME Jeffers, G Czerwinski, CJ Michejda,

GF Vande Woude (NCI)

Serial No. 60/075,994 filed 26 Feb 98

Licensing Contact: Jaconda Wagner, 301/496–7735 ext. 284

HGF/SF, which is the ligand for the tyrosine kinase receptor encoded by the c-Met proto-oncogene, is involved in tumor establishment, progression and metastasis. HGF/SF is synthesized as a 90 kDa single chain precursor polypeptide (pro-HGF/SF) which is devoid of biological activity. The critical step in HGF/SF activition is proteolytic cleavage generating an β heterodimer in which an β chain of 60 kDa and a β chain of 32–36 kDa are bound to one another by a disulfide bridge. The cleavage/activation of pro-HGF/SF represents the initial stage of HGF/SF-met activation and provides a possible point for interference by potential inhibitors.

This invention is based on the discovery that suramin and related polysulfonated compounds inhibit cleavage of pro-HGF/SF. The invention provides an efficient assay for identifying inhiitors of HGF/SF activation. The invention also describes suramin-like compounds that can be used to inhibit HGF/SF activation, thereby inhibiting tumor growth and metastasis. These compounds are less toxic than comparable molecules.

Vaccines For Blocking Transmission of Plasmodium vivax

DC Kaslow, T Tsuboi, M. Torii (NIAID)

Serial No. 60/067,596 filed 05 Dec 97

Licensing Contact: Carol Salata, 301/496–7735 ext. 232

This invention relates to novel methods and compositions for blocking transmission of Plasmodium vivax which cause malaria. In particular, Pvs25 and Pvs28 polypeptides, variants and fusion proteins thereof, are disclosed which, when administered to a susceptible organism, induce an immune response against a 25 kD and 28 kD protein, respectively, on the surface of *Plasmodium vivax* zygotes and ookinetes. This immune response in the susceptible organism can block transmission of malaria.

Stromal Cell Derived Factor-1 (SDF–1) And Method of Use For Diagnostic And Prognostic Indicator Or AIDS Pathogenesis

C. Winkler, S O' Brien (NCI)

Serial No. 60.063,832 filed 30 Oct 97

Licensing Contact: Carol Salata, 301/496–7735 ext. 232

Stromal cell derived factor-1 (SDF–1) is the principal ligand for CXCR4 (a 7-transmembrane G/coupled receptor) which, with CD4, provides an entry port for T-tropic HIV–1, a variety that frequently develops in AIDS patients just prior to T-lymphocyte depletion. This invention is based on the discovery of a correlation between the presence of a mutation at one nucleotide position of the 3′untranslated region of the SDF1 gene and delayed progression to AIDS and death due to HIV infection. Based on this discovery, it is the object of the present invention to provide diagnostic and therapeutic approaches to treating HIV infection by diagnosing the mutation and down regulating the CXCR4 receptor with native or synthetic SDF–1.

Recominant Adenoviral Targeting Vector

SE Spence, JR Keller, JS Smith (NCI)

Serial No. 60/061,587 filed 10 Oct 97

Licensing Contact: Elaine Gese, 301/496–7056 ext. 282

The current invention embodies recombinant adenoviral vectors for use in targeted gene transfer. The method by which these vectors are generated involves no molecular modifications to the adenovirus genome, and allows for the production of vectors targeted specifically to virtually any cell line of choice. Specifically, the vectors are generated by directly linking biotin to the capsid of advenovirus particles. The particles are then treated with streptavidin and subsequently incubated with a biotinylated targeting moiety which is capable of recognizing a specific marker which is expressed on the surface of selected cells.

The resulting adenoviral vectors would appear to be of value for use in gene transfer, and can be targeted to virtually any cell type of interest via incubation with a specific targeting moiety.

To date, the inventors have demonstrated that these vectors can be specifically directed to target and infect hematopoietic cell lines which display the c-kit receptor, and are capable of achieving high levels of expression in these cell lines. Also, these vectors can be specifically directed to cell surface markers such as CD34, CD 44 and others through antibodies directly attached to the biotynilated adenoviral vectors. Such gene transfer may represent a potential means by which various diseases, including immunodeficiency diseases, blood cell disorders, AIDS, and various cancers, could be treated. Therefore, the current invention appears to represent a novel gene therapy approach upon which the development of specific therapies against a broad range of diseases may be based.

Recombinant Proteins of a Pakistani Strain of Hepatitis E and Their Use in Diagnostic Methods and Vaccines

SA Tsarev, SU Emerson, RH Purcell (NIAID)

Serial No. 08/809,523 filed 28 Jun 97; PCT filed

Licensing Contact: Carol Salata, 301/496–7735, ext. 232

A strain of hepatitis E virus from Pakistan (SAR–55) implicated in an epidemic of enterically transmitted non-A, non-B hepatitis, now called hepatitis E, is disclosed. The invention relates to the expression of the whole structural region of SAR–55, designated open reading frame 2 (ORF–2), in a eukaryotic expression system. The expressed protein is capable of forming HEV virus-like particles which can serve as an antigen in diagnostic immunoassays and as an immunogen or vaccine to protect against infection by hepatitis E.

Chimeric Gag Pseudovirions

GJ Tobin, MA Gonda (NCI)

Serial No. 08/857,385 filed 15 May 97

Licensing Contact: J. Peter Kim, 301/496–7056 ext. 264

The human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS). The HIV virion basically consists of a viral core and envelope. The core consists predominantly of gag- and pol-encoded proteins and the viral RNA. Expression of recombinant Gag precursor proteins can lead to assembly and budding of virus-like particles (pseudovirions). The production of Gag-based pseudovirions in mammalian and insect cell systems using recombinant virus vectors provides a novel technology for engineering recombinant protein-based particulate vaccines for HIV and other viruses. The incorporation of additional viral or cellular, peptides and polypeptides may be advantageous in vaccine

preparations, since they may contain antigenic epitopes that may play a role in inducing protection from infection or disease.

The subject invention provides chimeric nucleic acids comprising a retroviral gag sequence, a target nucleic acid sequence derived from a nucleic acid encoding a fusion partner, and a frame shift site. Expression of the chimeric gene cassette results in packaging the fusion partner into the Gag pseudovirion. Suitable fusion partners can be derived from any protein of interest which has a biological activity or which elicits a cellular or humoral immune response.

Method For Measuring Mechanical Properties of the Collagen Network in Cartilage

PJ Basser, A Maroudas (NICHD)

Serial No. 60/038,005 filed 14 Feb 97; PCT/US98/02727 filed 17 Mar 98

Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present application describes a methodology for assessing the mechanical integrity of extracellular matrices such as cartilage. Specifically, the invention teaches how to characterize the mechanical integrity of the collagen network as well as the swelling properties of the proteoglycans trapped within it. This is done by performing an osmotic stress titration experiment on a tissue specimen, and interpreting the results using a simple mathematical model. This invention provides the necessary experimental and theoretical tools to understand functional consequences of: (1) endogenous changes in cartilage structure that occur normally due to growth or aging; (2) exogenous changes in cartilage structure due to the addition of biochemical agents or caused by genetic manipulations; and (3) inherent differences between cartilage specimens that are obtained from different joints within the same subject or from different subjects. These methods can also be applied to characterize the mechanical integrity of tissue cultured or ''tissue engineered'' cartilage.

Vectors for Delivering Viral and Oncogenic Inhibitors

SM Rybak, A Cara, GL Gusella, DL Newton (NCI)

Serial No. 60/022,052 filed 22 Jul 96; PCT/US97/12637 filed 17 Jul 97

Licensing Contact: Carol Salata, 301/496–7735, ext. 232

The invention concerns cell transduction vectors which are capable of inhibiting viral replication in cells transduced with these vectors, and which also are capable of inhibiting the growth of cancer cells. Specifically, these expressions vectors produce protective genes which interfere with viral replication. These genes are tightly regulated by HIV–1 Tat and Rev proteins, which if produced after infection can induce expression of the protective genes. The vectors contain either a single gene (delta-gag), or a combination of two different genes (delta-gag and RNAse) which interfere with HIV–1 replication at different stages of the HIV–1 life cycle. Following transduction of target cells, the mRNA for the protective genes is incorporated into the newly budding virion along with the viral genomic mRNA. Following infection of neighboring cells, the mRNA for the protective gene can be reverse transcribed and integrated into these cells, thereby increasing the proportion of cells containing the protective gene.

In providing protection against viral replication, the vectors embodied in this invention could be used in gene therapy against HIV and against other viral diseases. In addition, the vectors could be used for introducing specific genes into neoplastic cells and thereby be effective in treating cancer and other diseases.

Anti-Viral Pharmaceutical Compositions Containing 1,2–Dithiane Compounds and Methods of Using Thereof

WG Rice, R Schultz, D Baker, LE Henderson (NCI)

Serial No. 60/021,665 filed 05 July 96; PCT/US97/10870 filed 03 Jul 97

Licensing Contact: J. Peter Kim, 301/496–7056 ext. 264

Certain highly conserved structures, known as retroviral-type CCHC zinc fingers, are found in the nucleocapsid proteins of all retroviruses, including HIV–1 and HIV–2. It is known that these zinc finger structures perform essential functions in viral infection and replication.

The subject invention provides for pharmaceutical compositions comprising dithiane dioxide compounds which are useful as antiviral agents and are particularly effective at inhibiting the replication of retroviruses and for treating retroviral pathologies. The 1,2–dithiane compounds target the zinc fingers of the nucleocapsid protein. These compositions represent potential agents for prevention and treatment of HIV and of other retroviral diseases. The subject invention also embodies methods for the administration of these compositions, a kit containing these compositions, and methods for the inactivation of contaminating retrovirus in samples of potentially infected body fluids.

Dated: September 3, 1998.

Jack Spiegel,

Diretor, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 98–24368 Filed 9–10–98; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Neurological Disorders and Stroke; Notice of 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 a meeting of the Board of Scientific Counselors, National Institute of Neurological Disorders and Stroke.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public as indicated below in accordance with the provisions set forth in section 552b(c)(6), Title 5 U.S.C., as amended for the review, discussion, and evaluation of individual intramural programs and projects conducted by the National Institute of Neurological Disorders and Stroke, including consideration of personnel qualifications and performance, and the competence of individual investigators, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Board of Scientific Counselors, National Institute of Neurological Disorders and Stroke October 4–6, 1998.

Date: October 4–6, 1998.

Closed: October 4, 1998, 7:00 PM to 10:00 PM.

Agenda: To review and evaluate personal qualifications and performance, and competence of individual investigators.

Place: National Institutes of Health, Building 31, Conference Room 6C9, 31 Center Drive, Bethesda, MD 20892.

Open: October 5, 1998, 8:00 AM to 4:30 PM.

Agenda: To discuss program planning and program accomplishments.