## 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 an agency 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.

**Methylation Inhibitor Compounds**

Victor Marquez *et al.* (NCI).
U.S. Provisional Application No. 60/547,902
Filed 25 Feb 2004
(DHHS Reference No. E–074–2004/0–US–01).
*Licensing Contact:* Jeff Walenta; 301/435–4633; *walentaj@mail.nih.gov.*

Aberrant *de novo* DNA methylation is commonly associated with cancer. Several studies have shown that *de novo* methylation of tumor suppressor genes can lead to silencing of these genes and abnormal growth of cancer cells. Therefore, DNA methylation inhibitors may be used in cancer therapy to modulate hypermethylation of genes and to reactivate anti-proliferative, apoptotic and differentiation-inducing genes in cancer cells. Although some compounds have been proposed for use as DNA methylation inhibitors, these compounds are chemically instable, have weak potency and can generate toxic metabolites, thus preventing them being used as therapeutic agents.

The present invention relates to compositions and compounds that are useful as DNA methylation inhibitor compounds. The invention also relates to a method, using these compositions and compounds, of treating various cancers having a silenced tumor suppressor gene, and a method of treating a DNA-methylation-mediated disease. These compounds are generally chemically stable, non-toxic and may be administered orally or by injection. A method of making a compound is described.

These compounds seem to have a better therapeutic profile than another published DNA methylation inhibitor, Zebularine.

**A Combined Immunosuppressive Therapy Consisting of Glucocorticoid and rIL–2**

Xin Chen *et al.* (NCI).
U.S. Provisional Application No. 60/515,217
Filed 27 Oct 2003
(DHHS Reference No. E–211–2003/0–US–01).
*Licensing Contact:* Mojdeh Bahar; 301/435–2950; *baharm@mail.nih.gov.*

The invention is a combination immunosuppressive therapeutic regimen consisting of a glucocorticoid and rIL–2. The combination minimizes the side effects associated with glucocorticoid treatment, and is useful in inhibiting or treating inflammation, immune-mediated disorders, and transplant rejection. The treatment regimen at once promotes cell death of CD4+CD25– T effector cells, including cytotoxic T cells, and expansion of inhibitory Foxp3+CD4–CD25+ T regulatory ($T_{reg}$) cells. This regimen involves application of both glucocorticoid and IL–2, and is based on the surprising observation that IL–2 selectively protects $T_{reg}$ cells from glucocorticoid-induced cell death. As $T_{reg}$ cells inhibit CD4+CD25– T cells, the effect of combined glucocorticoid/IL–2 therapy is to enhance the immunosuppressive effect of the glucocorticoids. In this context, glucocorticoids and IL–2 act synergistically to suppress cellular immune responses.

**Production of Adeno-Associated Viruses in Insect Cells**

Robert M. Kotin *et al.* (NHLBI).
U.S. Patent No. 6,723,551
Issued 20 April 2004
(DHHS Reference No. E–325–2001/1–US–01).
*Licensing Contact:* Jeff Walenta; 301/435–4633; *walentaj@mail.nih.gov.*

Adeno-associated virus (AAV) is being developed for gene therapy applications. This virus type presents several advantages over alternate vectors for therapeutic gene delivery. AAV is not considered pathogenic and transduces stably dividing and non-dividing cells. AAV also shows good serotype specificity to various cell types for targeted gene delivery.

The present invention describes a highly scalable adeno-associated virus (AAV) vector production method in insect cells. The system for producing recombinant AAV (rAAV) uses the AAV Rep protein and an AAV ITR. This production method produces virus particles much more efficiently than the standard mammalian cell culture system. Yields of rAAV produced in Sf9 cells exceed 10e15 per liter for some constructs. The improvement in production efficiency translates into lower production costs and potential for commercial scale manufacturing. In addition, all serotypes of AAV can be produced, with the respective AAV serotype vectors available for the immediate scale up of AAV production.

This technology will give a company producing large quantities of AAV a significant competitive advantage over traditional AAV production methods.

**B-Homoestra-1,3,5(10)-trienes as Modulators of Tubulin Polymerization**

Ernest Hamel *et al.* (NCI).
U.S. Patent No. 6,696,436
Issued 24 Feb 2004
(DHHS Reference No. E–230–1999/0–US–03).
*Licensing Contact:* Jeff Walenta; 301/435–4633; *walentaj@mail.nih.gov.*

This invention relates to the general field of steroid chemistry, particularly to estrone derivatives. Specifically, this invention provides B-ring expanded estra-1,3,5(10)-triene compounds of general formula which modulate the polymerization of tubulin and/or the depolymerization of microtubules. Successful cell division, as a step of cell mitosis, depends on the proper polymerization of tubulin and the proper depolymerization of microtubules. This invention also relates to methods of using the compounds as anti-mitotic, anti-angiogenic and anti-tumor therapeutics for the treatment of cancer or other mammalian diseases characterized by undesirable angiogenesis. Additionally, the invention provides methods of preparing the compounds. The compounds of the invention are also expected to have utility as research tools.

This invention was published in: Verdier-Pinard *et al.*, ''A Steroid Derivative With Paclitaxel-Like Effects on Tubulin Polymerization,'' Mol. Pharmacol. 2000 Mar, 57(3):568–575; Wang *et al.*, ''Synthesis of B-ring Homologated Estradiol Analogues that Modulate Tubulin Polymerization and

Microtubule Stability,'' J. Med. Chem. 2000 Jun 15, 43(12):2419–2429.

**Methods and Compositions for Transforming Dendritic Cells and Activating T Cells**

Patrick Hwu *et al.* (NCI).

U.S. Patent No. 6,734,014

Issued 11 May 2004

(DHHS Reference No. E–040–1996/0–US–07).

*Licensing Contact:* Jeff Walenta; 301/435–4633; *walentaj@mail.nih.gov*.

T cells mediate most forms of cellular immunity. Typically T cells do not respond to free antigenic peptides, but instead T cells interact with a specialized set of cell surface proteins, which are the class I and class II major histocompatibility complexes, or MHC. Specialized antigen-presenting cells, such as macrophage and dendritic cells, present antigenic peptides on the surface cells in conjunction with the MHC molecules, and induce cytotoxic T cells to proliferate. T cells are induced by these antigen-presenting cells to recognize corresponding antigens expressed on MHC antigens on the surface of target cells, and destroy these target cells.

This invention describes a novel method for making transformed dendritic cells with any recombinant nucleic acid, which have been difficult to transduce using existing methods. Recombinant dendritic cells are made by transforming a stem cell and differentiating the stem cell into a dendritic cell. The resulting dendritic cell is an antigen-presenting cell that activates T cells against MHC class I-antigen targets. The present invention provides a valuable tool for the treatment of cancer, and viral and parasitic infections using the recombinant dendritic cells. The invention also provides therapeutic compositions and pharmaceutical compositions.

This research is described in Reeves *et al.*, ''Retroviral Transduction of Human Dendritic Cells with a Tumor-Associated Antigen Gene,'' Cancer Res. 1996 Dec15, 56(24):5672–5677.

Dated: August 18, 2004.

**Steven M. Ferguson,**

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

[FR Doc. 04–19539 Filed 8–25–04; 8:45 am]

**BILLING CODE 4140–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

### Clinical Center; Notice of Meeting

Pursuant to section 10(a) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the NIH Advisory Board for Clinical Research.

The meeting will be open to the public, 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.

*Name of Committee:* NIH Advisory Board for Clinical Research.

*Date:* September 21, 2004.

*Time:* 2 p.m. to 6 p.m.

*Agenda:* For discussion of planning, operational, and clinical research issues.

*Place:* National Institutes of Health, Building 1, 1 Center Drive, Room 151, Bethesda, MD 20892.

*Contact Person:* Maureen E. Gormley, Executive Secretary, Warren Grant Magnuson Clinical Center, National Institutes of Health, Building 10, Room 2C146, Bethesda, MD 20892, 301/496–2897.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

Dated: August 19, 2004.

**LaVerne Y. Stringfield,**

*Director, Office of Federal Advisory Committee Policy.*

[FR Doc. 04–19548 Filed 8–25–04; 8:45 am]

**BILLING CODE 4140–01–M**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

### Fogarty International Center; 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 Fogarty International Center Advisory Board.

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 in accordance with the provisions set forth in sections 552b(c)(4) and 552(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:* Fogarty International Center Advisory Board.

*Date:* September 14, 2004.

*Open:* 8:30 a.m. to 12 p.m.

*Agenda:* A Report of the FIC Director on updates and overviews of new FIC initiatives. The main topics of the Board will be ''U.S. Attitudes Toward International Efforts.''

*Place:* National Institutes of Health, Lawton Chiles International House, Bethesda, MD 20892.

*Closed:* 1 p.m. to Adjournment.

*Agenda:* To review and evaluate grant applications.

*Place:* National Institutes of Health, Lawton Chiles International House, Bethesda, MD 20892.

*Contact Person:* Jean L. Flagg-Newton, Special Assistant to the Director, FIC.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

Information is also available on the Institute's/Center's home page: *http://www.nih.gov/fic/about/advisory.html,* where an agenda and any additional information for the meeting will be posted when available.

(Catalogue of Federal Domestic Assistance Program Nos. 93.106, Minority International Research Training Grant in the Biomedical and Behavioral Sciences; 93.154, Special International Postdoctoral Research Program in Acquired Immunodeficiency Syndrome; 93.168, International Cooperative Biodiversity Groups Program; 93.934, Fogarty International Research Collaboration Award; 93.989, Senior International Fellowship Awards Program, National Institutes of Health, HHS)

Dated: August 19, 2004.

**LaVerne Y. Stringfield,**

*Director, Office of Federal Advisory Committee Policy.*

[FR Doc. 04–19547 Filed 8–25–04; 8:45 am]

**BILLING CODE 4140–01–M**