on NIDA's evaluation of the information, capacities, and plans provided by potential Collaborator(s).

NIDA follows stepwise development processes and procedures common to the medications development paradigm, *i.e.*, a candidate compound must successfully complete each necessary pre-requisite step prior to being advanced for further testing and development. It is NIDA's intention to provide, assuming pre-requisite preclinical and clinical safety, preclinical and clinical trials services sufficient to permit the completion of Phase II hypothesis testing trials for cocaine and methamphetamine dependence indications. Assuming demonstration and review of safety and efficacy at the conclusion of Phase II trials and subject to negotiation, NIDA will consider undertaking Phase III trials sufficient to permit Collaborator to seek a U.S. New Drug Application (NDA).

Please note that a CRADA is not a funding mechanism. No NIH funding may be provided to a Collaborator under a CRADA. All assistance is provided ''in-kind''. Therefore the Collaborator will bear the financial and organizational costs of meeting its share of obligations under any Research Plan that may be negotiated in connection with the CRADA.

''Cooperative Research and Development Agreement'' or ''CRADA'' means the anticipated joint agreement to be entered into by NIDA pursuant to the Federal Technology Transfer Act of 1986 and Executive Order 12591 of October 10, 1987 to collaborate on the specific research project described below.

The National Institute on Drug Abuse seeks an agreement with a pharmaceutical or biotechnology company for joint research, development, evaluation, and potential commercialization of vigabatrin for the treatment of cocaine and methamphetamine dependence.

The CRADA aims include the rapid publication of research results and the timely exploitation of commercial opportunities. The CRADA partner will enjoy rights of first negotiation for licensing Government rights to any inventions arising under the agreement and will advance funds payable upon signing the CRADA to help defray Government expenses for patenting such inventions and other CRADA-related costs.

The expected duration of the CRADA will be 3 to 5 years.

Selection criteria for choosing the CRADA partner will include but not be limited to:

1. Ability to collaborate with NIDA on further research and development of this technology in Phase I and Phase II clinical studies. All such studies will occur in the United States and under FDA IND rules. Demonstration of experience and expertise in this or related areas of technology and the ability to provide intellectual contribution to the ongoing research and development. Ability to accomplish objectives according to an appropriate timetable to be outlined in the Collaborator's proposal. At an absolute minimum, Collaborator must be able to provide vigabatrin and placebo sufficient to complete all clinical and preclinical studies required in the Research Plan.

2. Demonstration of the resources (facilities, personnel and expertise) necessary to perform research, development and commercialization of this technology.

3. Commitment of reasonable effort and resources on research, development and commercialization of this technology.

4. Expertise in the commercial development, production, marketing and sales of products related to this area of technology .

5. The level of financial support, if any, the Collaborator will supply for CRADA-related Government activities.

6. A willingness to cooperate with the National Institute on Drug Abuse in the publication of research results.

7. An agreement to be bound by the DHHS rules involving human subjects, patent rights and ethical treatment of animals.

8. A willingness to accept the legal provisions and language of the CRADA with only minor modifications (if any).

9. Provisions for equitable distribution of patent rights to any inventions made during the course of the subject CRADA research. Generally, the rights of ownership are retained by the organization which is the employer of the inventor, with (1) an irrevocable, nonexclusive, royalty-free license to the Government (when a company employee is the sole inventor) or (2) an option to negotiate an exclusive or nonexclusive license to the company on terms that are appropriate (when a Government employee is an inventor).

Dated: May 11, 2005.

**Steven M. Ferguson,**

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

[FR Doc. 05–10066 Filed 5–19–05; 8:45 am]

**BILLING CODE 4140–01–P**

## 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.

**Synthesis of Phosphocholine Ester Derivatives and Conjugates Thereof**

Louis J. Rezanka (NIA), U.S. Provisional Application No. 60/623,762 filed 29 Oct 2004 (DHHS Reference No. E–330–2004/0–US–01)

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

Available for licensing and commercial development is a method of synthesizing EPC (4-Nitrophenyl-6-(O-phosphocholine) hydroxyhexanoate) and methods of synthesizing phosphocholine analogues and the phosphocholine conjugates formed therefrom. These molecules have clinical and research applications as anti-microbial agents. Specifically, EPC conjugated to protein carriers has been demonstrated to generate a protective immune response to Streptococcus pneumoniae. The invention provides a process for EPC synthesis as well as for its reaction intermediates for use in synthesis.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

**Methods and Compositions for the ex vivo High-Throughput Detection of Protein/Protein Interactions**

Sankar Adhya and Amos Oppenheim (NCI), U.S. Provisional Application No. 60/629,933 filed 23 Nov 2004 (DHHS Reference No. E–264–2004/0–US–01)

*Licensing Contact:* Cristina Thalhammer-Reyero; (301) 435–4507; *thalhamc@mail.nih.gov.*

This invention relates to methods and compositions for the high-throughput detection of protein-protein interactions using a lambda phage display system. One of the central challenges in systems biology is defining the interactome, or set of all protein-protein interactions within a living cell, as a basis for understanding biological processes for early diagnosis of disease and for drug development. The invention provides a novel proteomic toolbox for high-throughput medical research based in combining phage lambda protein display and recent advances in manipulation of the phage's genome. The method uses the bacteriophage lambda vector to express proteins on its surface, and is based on the use of mutant phage vectors such that only interacting phages will be able to reproduce and co-infect an otherwise non-permissive host and produce plaques. The invention allows for the characterization of bacteriophage display libraries that could be easily adapted to be used in large-scale functional protein chip assays.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

**Coacervate Microparticles Useful for the Sustained Release Administration of Therapeutics Agents**

Phillip Heller (NIA), U.S. Provisional Application No. 60/602,651 filed 19 Aug 2004 (DHHS Reference No. E–116–2004/0–US–01)

*Licensing Contact:* Susan O. Ano; (301) 435–5515; *anos@mail.nih.gov.*

The described technology is a biodegradable microbead or microparticle, useful for the sustained localized delivery of biologically active proteins or other molecules of pharmaceutical interest. The microbeads are produced from several USP grade materials, a cationic polymer, an anionic polymer and a binding component (*e.g.*, gelatin, chondroitin sulfate and avidin), in predetermined ratios.) Biologically active proteins are incorporated into preformed microbeads via an introduced binding moiety under nondenaturing conditions.

Proteins or other biologically active molecules are easily denatured, and once introduced into the body, rapidly cleared. These problems are circumvented by first incorporating the protein into the microbead. Microbeads with protein payloads are then introduced into the tissue of interest, where the microbeads remain while degrading into biologically innocuous materials while delivering the protein/drug payload for adjustable periods of time ranging from hours to weeks. This technology is an improvement of the microbead technology described in U.S. Patent No. 5,759,582.

This technology has two commercial applications. The first is a pharmaceutical drug delivery application. The bead allows the incorporated protein or drug to be delivered locally at high concentration, ensuring that therapeutic levels are reached at the target site while reducing side effects by keeping systemic concentration low. The microbead accomplishes this while protecting the biologically active protein from harsh conditions traditionally encountered during microbead formation/drug formulation.

The microbeads are inert, biodegradable, and allow a sustained release or multiple-release profile of treatment with various active agents without major side effects. In addition, the bead maintains functionality under physiological conditions.

Second, the microbeads and microparticles can be used in various research assays, such as isolation and separation assays, to bind target proteins from biological samples. A disadvantage of the conventional methods is that the proteins become denatured. The denaturation results in incorrect binding studies or inappropriate binding complexes being formed. The instant technology corrects this disadvantage by using a bead created in a more neutral pH environment. It is this same environment that is used for the binding of the protein of interest as well.

**Lepirudin Adsorbed to Catheter**

McDonald Horne (CC), U.S. Provisional Application No. 60/436,439 filed 23 Dec 2002 (DHHS Reference No. E–295–2002/0–US–01); PCT Application No. PCT/US03/40888 filed 22 Dec 2003, which published as WO 2004/058324 A2 on 15 Jul 2004 (DHHS Reference No. E–295–2002/0–PCT–02)

*Licensing Contact:* Michael Shmilovich; (301) 435–5018; *shmilovm@mail.nih.gov.*

The invention is a method for preventing venous access device (VAD) thrombosis by coating the VAD catheter with lepirudin, which has been found to be readily adsorbed by the silicone rubber of the VADs, and is expected to have good retention properties. VADs typically remain in place for weeks or months and sometimes cause clotting (thrombosis) of the veins. Accordingly, the simple technique of soaking a silicone catheter in lepirudin before venous insertion is the gist of the invention. Chronically ill patients who must be catheterized for long periods of time will benefit particularly from this technique which promises to reduce swelling and pain associated with VAD-induced thrombosis.

Reference: Horne, MK, Brokaw, KJ. Antithrombin activity of lepirudin adsorbed to silicone (polydimethylsiloxane) tubing. Thrombosis Research 2003; 112:111–115.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

**VAC–BAC Shuttle Vector System**

Bernard Moss, Arban Domi (NIAID), U.S. Provisional Application No. 60/371,840 filed 10 Apr 2002 (DHHS Reference No. E–355–2001/0–US–01); U.S. Provisional Application No. 60/402,824 filed 09 Aug 2002 (DHHS Reference No. E–355–2001/1–US–01); International Patent Application No. PCT/US03/11183 filed 10 Apr 2003, which published as WO 03/087330 A2 on 23 Oct 2003 (DHHS Reference No. E–355–2001/2–PCT–01); U.S. Patent Application No. 10/959,392 filed 05 Oct 2004 (DHHS Reference No. E–355–2001/2–US–02); European Patent Application No. 037183431 filed 10 Apr 2003 (DHHS Reference No. E–355–2001/2–EP–03)

*Licensing Contact:* Robert M. Joynes; (301) 594–6565; *joynesr@mail.nih.gov.*

This invention relates to a VAC–BAC shuttle vector system for the creation of recombinant poxviruses from DNA cloned in a bacterial artificial chromosome. A VAC–BAC is a bacterial artificial chromosome (BAC) containing a vaccinia virus genome (VAC) that can replicate in bacteria and produce infectious virus in mammalian cells.

The following are some of the uses for a VAC–BAC:

1. VAC–BACs can be used to modify vaccinia virus DNA by deletion, insertion or point mutation or add new DNA to the VAC genome with methods developed for bacterial plasmids, rather

than by recombination in mammalian cells.

2. It can be used to produce recombinant vaccinia viruses for gene expression.

3. It can be used for the production of modified vaccinia viruses that have improved safety or immunogenicity.

Advantages of the VAC–BAC shuttle system:

1. VAC–BACs are clonally purified from bacterial colonies before virus reconstitution in mammalian cells.

2. Manipulation of DNA is much simpler and faster in bacteria than in mammalian cells.

3. Modified genomes can be characterized prior to virus reconstitution.

4. Only virus with modified genomes will be produced so that virus plaque isolations are not needed.

5. Generation of a stock of virus from a VAC–BAC is accomplished within a week rather than many weeks.

6. Multiple viruses can be generated at the same time since plaque purification is unnecessary.

References:

1. Domi, A., and B. Moss. 2002. Cloning the vaccinia virus genome as a bacterial artificial chromosome in Escherichia coli and recovery of infectious virus in mammalian cells. Proc. Natl. Acad. Sci. USA 99:12415–12420.

2. Domi, A., and B. Moss. 2005. Engineering of a vaccinia virus bacterial artificial chromosome in Escherichia coli by bacteriophage lambda-based recombination. Nature Methods 2:95–97.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Dated: May 12, 2005.

**Steven M. Ferguson,**

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

[FR Doc. 05–10064 Filed 5–19–05; 8:45 am]

**BILLING CODE 4140–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

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**DU145 Camptothecin (CPT)-Resistant Cell Line**

Dr. Yves Pommier (NCI)
DHHS Reference No. E–159–2005/0—Research Tool
*Licensing Contact:* John Stansberry; 301/435–5236; *stansbej@mail.nih.gov*

Drug resistance is a major limitation of chemotherapy. Understanding how drug resistance develops may lead to more effective treatments. This invention describes the DU145 Camptothecin (CPT)-resistant prostate cancer cell line that can be used to study mechanisms of drug resistance. For more details see Pommier et al., Cancer Research 61, 1964–1969, March 1, 2001.

**Mammary Gland Differentiation by 2-Methoxyestradiol**

Jeffrey E. Green et al. (NCI)
DHHS Ref. No. E–069–2005/0–US–01
*Licensing Contact:* Thomas P. Clouse; 301/435–4076; *clouset@mail.nih.gov*

This invention is based on the discovery that administration of 2-Methoxyestradiol (2-ME2) to female mice at various developmental stages will result in the differentiation of mammary epithelial cells to form rudimentary alveolar structures and to produce milk proteins. This effect has also been demonstrated in an in vitro experimental system. Since 2-ME2 is highly expressed during late stages of human pregnancy and pregnancy is known to reduce the risk of human bresat cancer, possibly due to differentiating effects on the mammary gland, 2ME2 may be developed into a preventive agent against breast cancer in women. Additionally, 2-ME2 may be useful in augmenting mammary gland differentiation and milk production under circumstances where normal differentiation is compromised.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

**Methods for Detecting Progression of Low Grade Cervical Dysplasia**

Thomas Ried et al. (NCI)
DHHS Reference No. E–041–2005/0–US–01
*Licensing Contact:* Thomas P. Clouse; 301/435–4076; *clouset@mail.nih.gov*

This invention describes a test that can be applied to Pap smears to differentiate low-grade dysplastic lesions that are likely to progress to higher-grade dysplasia and cervical cancer from those that are likely to regress. The differentiating factor is the presence of genetic gain on the long arm of chromosome 3. The inventors have shown that low grade Pap smears that progress already exhibit extra copies of 3q, while those that do not show the 3q gain spontaneously regress.

Around 10–15% of the 3 million Pap smears with low-grade dysplasia each year in the United States progress to higher grade lesions. Currently, HPV testing is used to stratify these low grade disease Pap smears, but as the majority of these Pap smears are already HPV infected, the test has very low specificity. The instant 3q test, which targets the human telomerase gene, TERC, is a significant improvement in sensitivity and specificity over the current methods used for the detection of progressing versus regressing lesions.

**Antibodies to Rheb, a Ras-Related Protein**

Geoffrey J. Clark and Michele Vos (NCI)
DHHS Reference No. E–351–2004—Research Tool.
*Licensing Contact:* Mojdeh Bahar; 301/435–2950; *baharm@mail.nih.gov*

The invention relates to polyclonal antibodies that recognize the protein Rheb, a key player in protein biosynthesis. Rheb is a small GTP-binding protein that is structurally related to the oncoprotein Ras, but Rheb does not activate the same pathways as Ras. Instead, Rheb binds to the tumor suppressor TSC2 (Tuberin) and causes activation of the S6 kinase in a TOR (Target of Rapamycin) dependent manner. Rheb likely plays roles in the response to insulin and the development of human tumors. Thus, the antibodies could provide useful reagents to investigate the functions of Rheb in these and other biological processes.