requests to make oral presentations, to the contact person by April 14, 2005.

Transcripts: Transcripts of the meeting may be requested in writing from the Freedom of Information Office (HFI–35), Food and Drug Administration, 5600 Fishers Lane, rm. 12A–16, Rockville, MD 20857, approximately 15 working days after the meeting at a cost of 10 cents per page.

If you need special accommodations due to a disability, please contact Sema Hashemi at least 7 days in advance.

SUPPLEMENTARY INFORMATION: The ICH was established in 1990 as a joint regulatory/industry project to improve, through harmonization, the efficiency of the process for developing and registering new medicinal products in Europe, Japan, and the United States without compromising the regulatory obligations of safety and effectiveness.

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for medical product development among regulatory agencies. ICH was organized to provide an opportunity for harmonization initiatives to be developed with input from both regulatory and industry representatives. ICH is concerned with harmonization among the following three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labor, and Welfare; the Japanese Pharmaceutical Manufacturers Association; the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA; and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations. The ICH Steering Committee includes representatives from each of the ICH sponsors and Health Canada, the European Free Trade Area and the World Health Organization. The ICH process has achieved significant harmonization of the technical requirements for the approval of pharmaceuticals for human use in the three ICH regions.

The current ICH process and structure can be found at the following Web site: *http://www.ich.org*. (FDA has verified the Web site address, but we are not responsible for subsequent changes to the Web site after this document publishes in the **Federal Register**.)

Interested persons may present data, information, or views orally or in writing, on issues pending at the public meeting. Oral presentations from the public will be scheduled between approximately 1 p.m. and 2 p.m. Time allotted for oral presentations may be limited to 10 minutes. Those desiring to make oral presentations should notify the contact person by April 14, 2005, and submit a brief statement of the general nature of the evidence or arguments they which to present, the names and addresses, phone number, FAX, and e-mail of proposed participants, and an indication of the approximate time requested to make their presentation.

The topics to be discussed are the topics for discussion at the forthcoming ICH Steering Committee Meeting and ICH Expert Working Groups. One of the topics for the upcoming ICH meeting is an Efficacy Brainstorming Session focusing on the review of the existing efficacy guidelines and their need for updating as well as potential new topics for consideration. The complete set of ICH Efficacy Guidelines may be found at *http://www.ich.org/* or *http://www.fda.gov/cder/guidance/index.htm*. To promote a fuller discussion of this topic the public meeting will be expanded to include public input on initiatives related to current ICH efficacy guidelines and consider needs for further information both within and between existing guidances. These initiatives include electronic source data, clinical development plan summaries, Health Level 7 structured product labeling, and other initiatives including information exchange standards (e.g., eCTD and terminology standards).

The agenda for the public meeting will be made available on April 15, 2005, via the internet at *http://www.fda.gov/cder/meeting/ICH_Spring2005.htm*.

Dated: April 1, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–7020 Filed 4–5–05; 11:53 am]

BILLING CODE 4160–01–S

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.

Methods for High-Efficiency Single Genome Sequencing of HIV

Drs. John Coffin, Mary Kearney, Frank Maldarelli and Sarah E. Palmer (NCI), *et al.*

U.S. Provisional Application filed 25 Jan 2005 (DHHS Reference No. E–022–2005/0–US–01).

Licensing Contact: Sally Hu; 301/435–5606; *hus@mail.nih.gov*.

The invention is directed to a method for efficiently obtaining single genome sequences (SGS) of HIV from a biological sample. The invention has the following advantages over the current commercial genotyping in use: (1) It might improve the sensitivity of diagnosis of drug resistant HIV in newly infected HIV patients; (2) It might provide a more affordable diagnostic tool for early detection of drug resistance since the invention is adaptable to an automated approach for the high-throughput processing of a large number of patient sample; (3) It might improve patient outcome since SGS has the ability to identify low level mutation and will permit a more comprehensive evaluation of resistance in patients and might potentially change the clinical approach to treating resistant virus. In summary, this

invention might be a new important diagnostic tool for AIDS patients.

Reference: Sarah Palmer *et al.*, ''Multiple, Linked Human Immunodeficiency Virus Type 1 Drug Resistance Mutations in Treatment-Experienced Patients are Missed by Standard Genotype Analysis,'' J. Clin. Microbiol. (Jan 2005) 43(1):406–413.

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

HIV Neutralization by Structure-Based Enhancements of CD4-Molecular Mimicry

Peter D. Kwong, Chih-chin Huang, and Tongqing Zhou (NIAID), *et al.*

U.S. Provisional Patent Application No. 60/623,762 filed 29 Oct 2004 (DHHS Reference No. E–333–2004/0–US–01).

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

Available for licensing are compositions and methods for inhibiting CD4–gp120 interactions. HIV infectivity is mediated by interactions between the lymphocyte cellular protein CD4 and HIV exterior gp120 envelope glycoprotein. The invention presents crystal structures of a number of co-complexes between CD4 mimics, CD4M33, F23, and others disclosed herein, with gp120, as well as other mimics and molecules, which interact with gp120. CD4M33 has greater affinity than F23 for HIV–1 primary isolates, whereas F23 is a better mimic of CD4 and showed greater neutralization breadth than CD4M33 against diverse isolates from HIV–1, HIV–2, and SIVcpz. These results provide a basis for the development of anti-HIV antagonists with increased breadth of neutralization. Moreover, methods are disclosed for the identification of a mimic of CD4 with possible broad-spectrum activity. These methods can be used for drug screening and variant CD4 mimic production. Also, methods are provided for characterizing and evaluating protein structure, for designing candidate ligands, and for constructing CD4 mimetic antagonist or the interfacial cavity binding compounds.

Finally, provided are methods for producing mono- and polyclonal antibodies for use in vaccines. Mimics binding to gp120 cause conformational change in the protein, thus exposing epitope regions for antibody recognition. The uses of the mimetics and also of a mimetic-based immunogen in inhibiting, reducing, or preventing HIV infection are also discussed. Suggestions are presented for therapeutic uses of the antibodies in preventing a decline in CD4 T cell levels in HIV-positive patients.

Candidate DNA HIV Vaccine

Gary J. Nabel *et al.* (NIAID).

U.S. Provisional Application No. 60/588,378 filed 16 Jul 2004 (DHHS Reference No. E–267–2004/0–US–01).

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

NIH is pleased to announce as available for licensing technology related to HIV vaccines, which involves a vaccine candidate that is in phase I clinical trials. The subject technology is from a broad scientific program directed toward development of an HIV vaccine that will generate cellular and humoral immunity to HIV from different clades, which vary in regions throughout the world and which is a critical aspect to be addressed by an HIV vaccine to be administered worldwide. The vaccine candidate described herein is one of the first multiclade-component HIV vaccines to enter into clinical trials. This technology describes a candidate HIV vaccine comprising six DNA constructs, each expressing different HIV proteins, HIV Env from clades A, B, and C, and the Gag, Pol, and Nef proteins from clade B. Phase I clinical trials for this vaccine combination are currently underway. The DNA expression vectors described herein were designed to maximize protein expression levels. This technology offers a promising approach in the HIV vaccine field.

HIV Vaccine Immunogens and Immunization Strategies

Gilad Ofek *et al.* (NIAID).

U.S. Provisional Application No. 60/570,883 filed 14 May 2004 (DHHS Reference No. E–218–2004/0–US–01).

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

This invention relates to novel immunogens that generate an immune response against HIV–1 gp41 in mammals. The immunogens bind to the broadly neutralizing 2F5 monoclonal antibody as well as to antibodies 4E10 and Z13. The immunogens were designed based on structural considerations from peptide-2F5 complexes. These complexes were characterized and found to have specific features, necessary to elicit an antibody response. It has been difficult to elicit broadly neutralizing antibodies against HIV–1, and this technology offers a potential solution.

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

Template Methods and Devices for Preparing Sample Arrays

Stephen Hewitt (NCI).

U.S. Patent Application No. 10/928,656 filed 26 Aug 2004 (DHHS Ref. E–098–2004–0–US–01).

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

Available for licensing and commercial development is a simple and inexpensive device and method for preparing tissue microarrays. The method includes placing a template defining an array of openings over a surface of the recipient block with receptacle holes, such that a needle or punch that contains a sample can be inserted through the openings of the template and the sample is then inserted into the receptacle hole in the recipient block. Tissue microarrays can include hundreds or even thousands of about 1mm discs of tissue specimens, fixed and arranged on a single microscope slide. Currently available tools provide means to generate hundreds of copies of this kind of slide. However, the equipment currently available can be quite complex and expensive, and thus it is often beyond the resources of many researchers.

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

Chimeric HIV/SIV Polypeptide Trimers as HIV/AIDS Vaccine Candidates

Bernard Moss (NIAID).

U.S. Provisional Application No. 60/510,952 filed 10 Oct 2003 (DHHS Reference No. E–356–2003/0–US–01); PCT Application filed 12 Oct 2004 (DHHS Reference No. E–356–2003/0–PCT–02).

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

The technology describes recombinant chimeric polypeptides of HIV Env in which all or part of the N-terminal portion (85 amino acids) of gp41 is replaced with the corresponding region of SIV. These chimeric polypeptides may be potential HIV/AIDS vaccine candidates. The substitution described above promotes efficient trimerization of the Env protein, which has been found in functional virions to have almost exclusively a trimeric structure. Therefore, by mimicking native HIV structure, the chimeric polypeptides

described in this technology could be used as immunogens for the generation of neutralizing antibodies that would bind to native HIV. The chimeric polypeptide that contains only the N-terminal portion of SIV in an HIV–1 background is particularly interesting, because several broadly neutralizing HIV–1 epitopes are present in the C-terminal segment of gp41.

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

Antibodies Against the Amino Terminus Region of Circumsporozoite Protein Prevent the Onset of Malaria

Dharmendar Rathore, Thomas McCutchan (NIAID).

U.S. Provisional Application No. 60/532,676 filed 23 Dec 2003 (DHHS Reference No. E–176–2003/0–US–01); PCT filed.

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

Malaria is one of the 5 major diseases of the world and a leading cause of childhood death in sub-Saharan Africa. Furthermore, the economic devastation of the disease is measured in the billions of dollars of lost wages and lowered productivity for the endemic areas of the world. In the U.S., it is a concern of travelers as well the military having to serve in those parts of the world. To date, there is no vaccine and one is not expected for another decade.

The invention presented here focuses on the ability of the malarial sporozoite to infect liver cells. Previous vaccines have focused on the carboxyl end of the circumsporozoite (CSP) protein and have few successes to show. This invention utilizes the finding that the amino terminal portion of the CSP protein is required for hepatic entry. The invention includes several CSP polypeptides and constructs encoding such polypeptides that have been shown to be required for hepatic entry for vaccine development, prevention and treatment are also claimed. Methods and kit claims are included for the detection of the CSP protein in biological samples as well as for the detection of circulating antibodies of the CSP protein are also included.

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

Determining Kinase Specificity

J.S. Shaw and Y. Liu (NCI).

U.S. Patent Application No. 10/660,370 filed 11 Sep 2003 (DHHS Reference No. E–054–2003/0–US–01) and International Application Number PCT/US04/029397 filed 10 Sep 2004 (DHHS Reference No. E–054–2003/1–PCT–01).

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

Available for licensing and commercial development are methods, articles, software and kits for determining the spectrum of peptidyl sequences that are recognized and phosphorylated by a kinase, such as those sites on proteins involved in signal transduction pathways. More specifically, the following is disclosed:

(a) Methods involving a degenerate library approaches to identify kinase specificity by identifying peptide sequences around such phosphorylation sites and ranking the peptides in preferential order after calculating a predictive score, such as the widely used position-specific scoring matrix (PSSM). The method also provides an informative graphical format for visually representing that information and software to output data in that format. The method provides significant improvements over other methods currently used for such purpose;

(b) Peptide sequences identified by the method of the invention, such as: (i) The spectrum of peptidyl sequences that are recognized and phosphorylated by a kinase, (ii) peptides that include kinase recognition sites and (iii) binding entities that specifically distinguish phosphorylated versus non-phosphorylated peptidyl sequences; and

(c) Kits for identifying kinase substrates including anti-peptide antibodies for research and diagnostic uses.

The technology is further described in: Fujii K, Zhu G, Liu Y, Hallam J, Chen L, Herrero J, Shaw S. 2004. Kinase peptide specificity: Improved determination and relevance to protein phosphorylation. Proc Natl Acad Sci USA 101:13744–9 (PMID: 15356339) and Zhu G, Fujii K, Belkina N, Liu Y, James M, Herrero J, Shaw S. 2005. Exceptional disfavor for proline at the P+1 position amongst AGC and CAMK kinases establishes reciprocal specificity between them and the proline-directed kinases. J Biol Chem 280:10743–8: (PMID: 15647260).

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

MVA Expressing Modified HIV Envelope, Gag, and Pol Genes

Bernard Moss (NIAID), Patricia Earl (NIAID), Linda Wyatt (NIAID), Leigh Anne Steinmeyer (EM), Thomas VanCott (EM), Matthew Harris (EM).

U.S. Provisional Application No. 60/459,175 filed 28 Mar 2003 (DHHS Reference No. E–023–2003/0-US–01); PCT Application filed 28 Mar 2004, which published as WO 2004/087201 on 14 Oct 2004 (DHHS Reference No. E–023–2003/0–PCT–02).

Licensing Contact: Peter Soukas; 301/435–4646; *soukasp@mail.nih.gov.*

This invention claims Modified Vaccinia Ankara (MVA), a replication-deficient strain of vaccinia virus, expressing Human Immunodeficiency Virus (HIV) env, gag, and pol genes, where the genes are isolated from Ugandan Clade D isolates, Kenyan Clade A isolates, and Tanzanian Clade C isolates. In a rhesus macaque SHIV model, DNA priming followed by a recombinant MVA (rMVA) booster controlled a highly pathogenic immunodeficiency challenge. Both the DNA and the rMVA components of the vaccine expressed multiple immunodeficiency virus proteins. Two DNA inoculations at zero (0) and eight (8) weeks and a single rMVA booster at twenty-four (24) weeks effectively controlled an intrarectal challenge administered seven (7) months after the booster. Additionally, the inventors have generated data showing that inoculations of rMVA induce good immune responses even without DNA priming.

The inventors are continuing preclinical work on the vaccine, and have generated further data on the vaccine. Furthermore, the inventors are continuing to optimize the vaccine by genetically modifying the genes. This vaccine will be the subject of an upcoming Phase I clinical trial. These findings provide hope that a relatively simple multiprotein DNA/MVA vaccine can help to control the Acquired Immune Deficiency Syndrome (AIDS) epidemic.

CC Chemokine Receptor 5 DNA, New Animal Models and Therapeutic Agents for HIV Infection

C. Combadiere, Y. Feng, E.A. Berger, G. Alkahatib, P.M. Murphy, C.C. Broder, P.E. Kennedy (NIAID).

U.S. Provisional Application No. 60/018,508 filed 28 May 1996 (DHHS Reference No. E–090–1996/0–US–01);

U.S. Patent Application No. 08/864,458 filed 28 May 1997 (DHHS Reference No. E–090–1996/0–US–04);

U.S. Patent Application No. 10/439,845 filed 15 May 2003 (DHHS Reference No. E–090–1996/0–US–05);
U.S. Patent Application No. 10/700,313 filed 31 Oct 2003 (DHHS Reference No. E–090–1996/0–US–06);
U.S. Patent Application No. 10/846,185 filed 14 May 2004 (DHHS Reference No. E–090–1996/0–US–07);
PCT Application No. PCT/US97/09586 filed 28 May 1997 (DHHS Reference No. E–090–1996/0–PCT–02);
European Patent Application No. 97929777.7 filed 28 May 1997 (DHHS Reference No. E–090–1996/0–EP–03).
Licensing Contact: Peter Soukas; 301/435–4646; *soukasp@mail.nih.gov.*

Chemokine receptors are expressed by many cells, including lymphoid cells, and function to mediate cell trafficking and localization. CC chemokine receptor 5 (CCR5) is a seven-transmembrane, G protein-coupled receptor (GPCR) which regulates trafficking and effector functions of memory/effector T-lymphocytes, macrophages, and immature dendritic cells. Chemokine binding to CCR5 leads to cellular activation through pertussis toxin-sensitive heterotrimeric G proteins as well as G protein-independent signalling pathways. Like many other GPCR, CCR5 is regulated by agonist-dependent processes which involve G protein coupled receptor kinase (GRK)-dependent phosphorylation, beta-arrestin-mediated desensitization and internalization.

Human CCR5 also functions as the main coreceptor for the fusion and entry of many strains of human immunodeficiency virus (HIV–1, HIV–2). HIV-1 transmission almost invariably involves such CCR5-specific variants (designated R5); individuals lacking functional CCR5 (by virtue of homozygosity for a defective CCR5 allele) are almost completely resistant to HIV–1 infection. Specific blocking of CCR5 (*e.g.* with chemokine ligands, anti-CCR5 antibodies, CCR5-blocking low MW inhibitors, etc.) inhibits entry/infection of target cells by R5 HIV strains. Cells expressing CCR5 and CD4 are useful for screening for agents that inhibit HIV by binding to CCR5. Such agents represent potential new approaches to block HIV transmission and to treat infected people. A small animal expressing both human CCR5 along with human CD4 supports entry of HIV into target cells, a necessary hurdle that must be overcome for development of a small animal model (*e.g.* transgenic mouse, rat, rabbit, mink) to study HIV infection and its inhibition.

The invention embodies the CCR5 genetic sequence, cell lines and transgenic mice, the cells of which coexpress human CD4 and CCR5, and which may represent valuable tools for the study of HIV infection and for screening anti-HIV agents. The invention also embodies anti-CCR5 agents that block HIV env-mediated membrane fusion associated with HIV entry into human CD4-positive target cells or between HIV-infected cells and uninfected human CD4-positive target cells.

This technology was reported in Alkhatib *et al.*, ''CC CKR5: a RANTES, MIP–1alpha, MIP–1beta receptor as a fusion cofactor for macrophage-tropic HIV–1,'' Science 272:1955–1958 (1996). The technology is available for exclusive or nonexclusive licensing.

Dated: March 25, 2005.

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

[FR Doc. 05–6895 Filed 4–6–05; 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.

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Identification of Molecular Markers for Endometriosis in Blood Lymphocytes Using DNA Microarrays

Idhaliz Flores (NHGRI), *et al.*

U.S. Provisional Application filed 18 Feb 2005 (DHHS Reference No. E–068–2005/0–US–01).
Licensing Contact: Marlene Shinn-Astor; (301) 435–4426; *shinnm@mail.nih.gov.*

Endometriosis is a common, non-malignant gynecological disease that affects up to 20% of women during their reproductive years. Endometriosis is characterized by the growth of endometrial tissue outside the uterus. This growth of tissue causes recurring severe pain and can lead to infertility. As the current procedure used for diagnosis is invasive and not entirely accurate, there is a need for a fast, accurate, and minimally invasive test to test for endometriosis.

Using DNA microarray analysis of blood lymphocytes, the inventors have identified two gene markers expressed in blood that are able to discriminate between those women who have endometriosis and those that don't. The two gene markers identified are interleukin-2 receptor gamma (IL–2RG, a component of cytokine receptors) and lysyl oxidase-like 1 (LOXL1, which plays an important role in collagen synthesis and has also been implicated as a growth regulatory gene). Other genes identified in the same manner and which also represent potential biomarkers for endometriosis await further validation studies.

The test would be minimally invasive and quick using a blood sample from the patient. Currently, patients must undergo a laparoscopy with the diagnosis dependent upon the expertise of the surgeon performing the procedure.

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

Increased Protein Production

Drs. Shankar Adhya and Sudeshna Kar (NCI).
U.S. Provisional Application No. 60/571,943 filed 18 May 2004 (DHHS Reference No. E–261–2003/0-US–01).
Licensing Contact: Pradeep Ghosh; (301) 435–5282; *ghoshpr@mail.nih.gov.*

There is a continuing market need to identify biological measures to enhance recombinant protein production for therapeutic inventions for the treatment of diseases. In general, the field of recombinant protein production, including inducement of protein production both by cloning and non-cloning methods and incorporation of antibiotic resistance genes in vectors appeared to be relatively crowded.