• U.S. Patents 6,051,405, 5,863,745, and 5,696,237 ''Recombinant Antibody-Toxin Fusion Protein'' [HHS Ref. E–135–1989/0];

• U.S. Patents 5,747,654, 6,147,203, and 6,558,672 entitled ''Recombinant Disulfide-Stabilized Polypeptide Fragments Having Binding Specificity'' [HHS Ref. E–163–1993/0];

• U.S. Patent 6,153,430, and U.S. Patent Application 09/684,599 ''Nucleic Acid Encoding Mesothelin, a Differentiation Antigen Present on Mesothelium, Mesotheliomas and Ovarian Cancers'' [HHS Ref. E–002–1996/0];

• U.S. Patent 6,083,502 entitled ''Mesothelium Antigen and Methods and Kits for Targeting It'' [HHS Ref. E–002–1996/1];

• U.S. Patent Application 09/581,345: ''Antibodies, Including Fv Molecules, and Immunoconjugates Having High Binding Affinity for Mesothelin and Methods for Their Use'' [HHS Ref. E–021–1998/0];

• U.S. Patent Application 10/297,337, ''Pegylation of Linkers Improves Antitumor Activity and Reduces Toxicity of Immunoconjugates'' [HHS Ref. E–216–2000/2];

• U.S. Patent Application 11/920,222 entitled ''Anti-Mesothelin Antibodies Useful For Immunological Assays'' [HHS Ref. E–015–2005/0];

• U.S. Patent Application 11/997,202 ''Mutated Pseudomonas Exotoxins with Reduced Antigenicity'' [HHS Ref E–262–2005/0]; and

• U.S. Patent Application 60/969,929 ''Deletions in Domain II of Pseudomonas Exotoxin A that Remove Immunogenic Epitopes without Affecting Cytotoxic Activity'' [HHS Ref. E–292–2007/0].

Licensing Status: The technology is available for exclusive and non-exclusive licensing.

Licensing Contact: David A. Lambertson, PhD; 301–435–4632; *lambertsond@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop immunotoxin SS1P. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: September 9, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–21506 Filed 9–15–08; 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, HHS.

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.

Compositions and Methods for Increasing Recombinant Protein Yields Through the Modification of Cellular Properties

Description of Technology: This technology relates to compositions and methods for improving the growth characteristics of cells engineered to produce biologically active products such as antibodies or glycosylated proteins. Featured is a method that uses gene candidates (e.g., cdkl3, siat7e, or lama4), or their expressed or inhibited products in cell lines, such as Human Embryonic Kidney (including HEK–293), HeLa, or Chinese Hamster Ovary (CHO). The gene expression modulates growth characteristics, such as adhesion properties, of the cell lines thereby increasing recombinant protein yields and reducing product production costs.

Applications: This technology may be used to improve production of therapeutic and/or diagnostic compounds, including therapeutic proteins or monoclonal antibodies from mammalian cells. Optimization of mammalian cells for use as expression systems in the production of biologically active products is very difficult. For certain applications, anchorage-independent cell lines may be preferred, whereas for other applications, a cell line that adheres to a surface, e.g., is anchorage-dependent, may be preferable. This technology provides a method for identifying a gene whose expression modulates such cellular adhesion characteristics. This method thus leads to an increase in the expression or yield of polypeptides, including therapeutic biologicals, such as antibodies, cytokines, growth factors, enzymes, immunomodulators, thrombolytics, glycosylated proteins, secreted proteins, and DNA sequences encoding such polypeptides and a reduction in the associated costs of such biological products.

Advantages: This technology offers the ability to improve yields and reduce the cost associated with the production of recombinant protein products through the selection of cell lines having:

- Altered growth characteristics.
- Altered adhesion characteristics.
- Altered rate of proliferation.
- Improvement in cell density growth.
- Improvement in recombinant protein expression level.

Market: Biopharmaceuticals, including recombinant therapeutic proteins and monoclonal antibody-based products used for in vivo medical purposes and nucleic acid based medicinal products now represent approximately one in every four new pharmaceuticals on the market. The market size has been estimated at $33 billion in 2004 and is projected to reach $70 billion by the end of the decade. The list of approved biopharmaceuticals includes recombinant hormones and growth factors, mAB-based products and therapeutic enzymes as well as recombinant vaccines and nucleic acid based products.

Mammalian cells are widely used expression systems for the production of biopharmaceuticals. Human embryo kidney (including HEK–293) and Chinese hamster ovary (CHO) are host cells of choice. The genes identified in this technology (e.g., cdkl3, sia7e, or lama4) can be used to modify these important cell based systems.

This technology is ready for use in drug/vaccine discovery, production and development. The technology provides methods for identification of specific gene targets useful for altering the production properties of either existing cell lines to improve yields or with new cell lines for the production of therapeutic and/or diagnostic compounds from mammalian cells.

Companies that are actively seeking production platforms based on mammalian cell lines that offer high

efficiency, high throughput systems for protein production or analysis at lower cost and ease of scale-up would be potential licensors of this technology.

Development Status: Late Stage—Ready for Production.

Inventors: Joseph Shiloach (NIDDK), Pratik Jaluria (NIDDK).

Related Publication: P. Jaluria *et al.* Application of microarrays to identify and characterize genes involved in attachment dependence in HeLa cells. *Metab Eng.* 2007 May;9(3):241–251.

Patent Status: PCT Application No. PCT/US2007/018699 filed 24 Aug 2007, which published as WO 2008/024459 on 28 Feb 2008; claiming priority to 24 Aug 2006 (HHS Reference No. E–149–2006/2–PCT–01).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov*.

Collaborative Research Opportunity: The National Institute of Diabetes and Digestive and Kidney Diseases, Biotechnology Core Laboratory, is seeking parties interested in collaborative research projects directed toward the use of this technology with cells for drug and vaccine production and development, including growth optimization, production and product recovery processes. For more information, please contact Dr. Joseph Shiloach, *josephs@intra.niddk.nih.gov*, or Rochelle S. Blaustein at *Rochelle.Blaustein@nih.gov.*

In Vitro Model for Hepatitis C Virion Production

Description of Technology: This invention provides an in vitro hepatitis C virus (HCV) replication system that is capable of producing viral particles in a culture medium. Hepatitis C is a major public health problem, the development of therapeutics for which has been hampered by a lack of a robust model system to study the complete viral life cycle. This invention provides a new model system for the complete replication cycle of hepatitis C virus and virion production, assembly and release. The model is useful for screening antiviral agents against HCV.

A full length HCV construct, CG1b of genotype 1b which is known to be infectious, was placed between two ribozymes designed to generate the exact 5′ and 3′ ends of HCV when cleaved. Using this system, HCV proteins and positive and negative RNA strands have been shown to reproduce intracellularly, and viral particles that resemble authentic HCV virions are produced and secreted into the culture medium.

The patent application includes claims directed toward the following: A construct comprising specific nucleic acid sequences including HCV genotype 1b, genotype 1a, genotype 2a or potentially other genotypes; a method for identifying a cell line that is permissive for infection with HCV; a method for propagating HCV in vitro; a method for screening agents capable of modulating HCV replication or activity; a method for testing the level of HCV replication or activity; a HCV vaccine comprising HCV virus particles.

Applications: The model offers a novel method for investigating the entire HCV life cycle including replication and pathogenesis and is useful for high-throughput antiviral screening. This technique may also be useful for making infectious particles that are useful in the production of HCV vaccines.

Advantages: This system provides a new, stable and efficient cell culture model to further study the life cycle and biology of HCV, and to test potential therapeutic targets for hepatitis C. This model has also been used to generate in cell culture HCV strains infectious for chimpanzees, the only experimental animal susceptible to infection with the hepatitis C virus, a critical step in the development of new vaccines for Hepatitis C.

Market: Hepatitis C virus (HCV) chronically infects approximately 200 million people worldwide and increases the risk of developing cirrhosis and hepatocellular carcinoma. This technology would be useful for studying the HCV life cycle, screening for therapeutic agents against multiple HCV strains, including Genotype 1a, 1b and 2a, and the development of HCV vaccines. HCV genotypes 1 and 2 are the major genotypes with worldwide distribution; they are known to be associated with different clinical profiles and therapeutic responses. Hence, the model may be used to screen for varying levels of effectiveness of therapeutics against the major HCV genotypes.

Development Status: This technology is available for use in diagnostics, drug/vaccine discovery, production and development. Current work is directed toward studies into the HCV life cycle and replication and the pathogenesis of HCV screening for antiviral agents against multiple HCV strains. This model has been used to generate in cell culture HCV strains infectious for chimpanzees, the only experimental animal susceptible to infection with the hepatitis C virus, a critical step in the development of new vaccines for Hepatitis C. Future work may be directed toward the use of this system for development of vaccine candidates against HCV.

Inventors: T. Jake Liang and Theo Heller (NIDDK).

Related Publications:

1. Z. Hu *et al.* Altered proteolysis and global gene expression in hepatitis B virus X transgenic mouse liver. J Virol. 2006 Feb;80(3):1405–1413.

2. T. Heller *et al.* An in vitro model of hepatitis C virion production. Proc Natl Acad Sci USA. 2005 Feb 15;102(7):2579–2583.

Patent Status: U.S. Patent Application No. 11/664,375 filed 30 Mar 2007, claiming priority to 30 Sep 2004 (HHS Reference No. E–324–2004/3–US–02).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute of Diabetes and Digestive and Kidney Diseases, Liver Diseases Branch, is seeking parties interested in collaborative research directed toward molecular strategies for vaccine and antiviral development, and animal models of viral hepatitis C. For more information, please contact Dr. T. Jake Liang at 301–496–1721 or *jliang@nih.gov* or Rochelle S. Blaustein at *Rochelle.Blaustein@nih.gov.*

Dated: September 9, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–21507 Filed 9–15–08; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

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