21R or anti-IL–21 monoclonal antibodies has been demonstrated to reduce TH2 immune responses associated with fibrosis in animal models.

The causes of chronic tissue fibrosis are diverse and the market for a therapeutic that targets fibrosis is large. Fibrosis is associated with diverse causes which include: genetic diseases (such as cystic fibrosis); autoimmune diseases (such as scleroderma); chronic viral infections (such as hepatitis), parasitic infections (such as schistosomiasis); and occupational exposures to causative agents (such as asbestosis). Additionally, many cases of tissue fibrosis are idiopathic.

Application: The treatment or amelioration of tissue fibrosis.

Inventors: Thomas A. Wynn (NIAID); Deborah A Young; Mary Collins; and Michael J. Grusby.

Relevant Publication: J Pesce *et al.* The IL–21 receptor augments Th2 effector function and alternative macrophage activation. J Clin Invest 2006 Jul;116(7):2044–2055.

Patent Status: U.S. patent application no. 11/402,885 (priority date April 14, 2005) and international patent applications including European patent application No. EP06/0750009 (HHS Reference No. E–250–2005).

Licensing Status: Available for non-exclusive licensing.

Licensing Contact: Surekha Vathyam, Ph.D.; 301–435–4076; *vathyams@mail.nih.gov*.

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this invention. Please contact Nicole Mahoney at 301–435–9017 or *mahoneyn@niaid.nih.gov* for more information.

Use of Discoidin Domain Receptor 1 (DDR1) and Agents That Affect the DDR1/Collagen Pathway

Description of Invention: Dendritic cells (DCs) are pivotal antigen-presenting cells for initiation of an immune response. Indeed, dendritic cells provide the basis for the production of an effective immune response to a vaccine, particularly for antigens wherein conventional vaccination is inadequate. DCs are also important in the production on an immune response to tumor antigens.

The present invention discloses methods of using the receptor tyrosine kinase discoidin domain receptor 1 (DDR1) to facilitate the maturation/differentiation of DCs or macrophages. Activating agents of DDR1 may be useful in the induction of highly potent, mature DCs or highly differentiated macrophages from DC precursors, such as monocytes. Use of this method may enhance the antigen presenting capabilities of the immune system, leading to a more effective overall immune response.

Inventor: Teizo Yoshimura (NCI).

Relevant Publications

1. H Kamohara *et al.* Discoidin domain receptor 1 isoform-a (DDR1a) promotes migration of leukocytes in three-dimensional collagen lattices. FASEB J. 2001 Dec;15(14):2724–2726.

2. W Matsuyama *et al.* Interaction of discoidin domain receptor 1 isoform b (DDR1b) with collagen activates p38 mitogen-activated protein kinase and promotes differentiation of macrophages. FASEB J. 2003 Jul;17(10):1286–1288.

Patent Status: U.S. Application No. 10/507,385 filed 09 Sep 2004 (HHS Reference No. E–083–2002/2–US–02).

Licensing Status: Available for licensing.

Licensing Contact: Betty B. Tong, Ph.D.; 301–594–6565; *tongb@mail.nih.gov*.

Dated: July 28, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–18504 Filed 7–31–09; 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.

A Tumorigenic MEF/3T3 Tet-Off Mouse Fibroblast Cell Line Stably Transfected With a T7–Tagged Srp20 Expression Construct (pJR17)

Description of Technology: Alternative RNA splicing is a means by which the human genome can produce many more proteins from the genes available. It is emerging that aberrations in alternative RNA splicing contributes to the development of cancers. SRp20 is a cellular splicing factor that is involved in the process of alternative splicing of RNA. Investigators at the National Cancer Institute (NCI), National Institutes of Health (NIH) have discovered that SRp20 is overexpressed in many types of cancer and furthermore promotes the induction and maintenance of tumor cell growth. This was demonstrated in part by engineering a non-tumorigenic cell to become tumorigenic in mice by overexpressing SRp20.

Research Material available for licensing is a tumorigenic MEF/3T3 tet-off mouse fibroblast cell line stably transfected with a T7-tagged SRp20 expression construct (pJR17) that is under the transcriptional control of tetracycline.

Applications: Use in pre-clinical development of therapeutic approaches to cancer that target aberrant alternative RNA splicing.

Advantages: Transcriptional control of expression using Tet-off system; Availability of stably transfected cell line saves time and effort for other investigators.

Market: Research Tool.

Development Status: Ready to use.

Inventors: Zhi-Ming Zheng and Rong Jia (NCI).

Publications: Manuscript in preparation.

Patent Status: HHS Reference No. E–229–2009/0—Research Material. Patent protection is not being sought for this technology.

Licensing Status: Available for licensing.

Licensing Contact: Sabarni Chatterjee, Ph.D.; 301–435–5587; *chatterjeesa@mail.nih.gov.*

Collaborative Research Opportunity: The National Cancer Institute, Center for Cancer Research, HIV and AIDS Malignancy Branch, is seeking statements of capability or interest from

parties interested in collaborative research to further develop, evaluate, or commercialize A Tumorigenic MEF/3T3 Tet-Off Mouse Fibroblast Cell Line Stably Transfected with a T7–Tagged Srp20 Expression Construct (pJR17). Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Truncated Methanocarba Adenosine Derivatives as A_3 Adenosine Receptor Antagonists

Description of Technology: Novel A_3 adenosine antagonists available for licensing. A_3 receptors are particularly highly expressed in inflammatory cells, making it a potentially desirable target for inflammatory diseases. This technology relates to highly specific antagonists and partial agonists of A_3 adenosine receptors, which are negatively coupled to adenylate cyclase and have been broadly implicated in inflammation, cardiovascular disease, and cancer. Further, A_3 adenosine receptors have been implicated in allergies, asthma, and chronic obstructive pulmonary disease.

Advantages: There are four known subtypes of adenosine receptors (A_1, A_{2A}, A_{2B}, and A_3). All are positively or negatively linked to cAMP, but have different distributions and different therapeutic potentials. In particular, the use of A_1 and A_2 selective ligands has been limited by the ubiquity of expression of the receptors throughout the body and the resultant side effects. On the other hand, high levels of A_3 receptor expression are limited to the CNS, testes, and the immune system. Thus, A_3 receptors represent a potentially highly specific target for treating related diseases.

Inventor: Kenneth A. Jacobson (NIDDK).

Related Publication: A Melman, B Wang, BV Joshi, ZG Gao, S de Castro, CL Heller, SK Kim, LS Jeong, KA Jacobson. Selective A_3 adenosine receptor antagonists derived from nucleosides containing a bicyclo[3.1.0]hexane ring system. Bioorg Med Chem. 2008 Sep 15;16(18):8546–8556.

Patent Status: U.S. Provisional Application No. 61/085,588 filed 01 Aug 2008 (HHS Reference No. E–285–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Steve Standley, Ph.D.; 301–435–4074; *sstand@mail.nih.gov*

Collaborative Research Opportunity: The NIDDK, Laboratory of Bioorganic Chemistry is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize A_3 adenosine receptor antagonists. Please contact Kenneth A. Jacobson, Ph.D. at *kajacobs@helix.nih.gov* or the NIDDK Office of Technology Transfer and Development at 301–451–3636 for more information.

Novel Proteins From the Sand Fly *Lutzomyia longipalpis* Are Potent Inhibitors of Complement Activity

Description of Technology: This invention relates to the discovery that five proteins from the salivary glands of *Lutzomyia longipalpis,* LJM04, LJM11, LJM19, LJM26, and LJL143, have anti-complement activity. These proteins demonstrate potent inhibition of both the classical and alternative pathways for complement activation. All proteins, excluding LJM19, were shown to bind and inhibit the C3b molecule, thus inactivating an integral component of the complement pathway.

The complement system is a very important line of defense against pathogens, and is involved in many pathologies and syndromes affecting human health. It is therefore envisioned that these five novel proteins may be used to treat conditions where the complement system is involved including lupus erythematosus, juvenile arthritis, and complications associated with cardiac surgery and hemodialysis.

Applications:

• Potent inhibition of complement activity.

• Treatment of diseases involving the complement system.

Development Status: Early Stage.

Inventors: Jesus G. Valenzuela *et al.* (NIAID).

Relevant Publication: RR Cavalcante, MH Pereira, NF Gontijo. Anti-complement activity in the saliva of phlebotomine sand flies and other haematophagous insects. Parasitology 2003 Jul;127(Pt 1):87–93.

Patent Status: U.S. Provisional Application No. 61/142,098 filed 31 Dec 2008 (HHS Reference No. E–205–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Jeffrey A. James, PhD; 301–435–5474; *jeffreyja@mail.nih.gov.*

Potent Anti-Coagulant Activity of a Novel Protein From the Sand Fly *Lutzomyia longipalpis*

Description of Technology: The salivary gland lysates of *Lutzomyia longipalpis,* the New World sand fly and main vector for visceral leishmaniasis, contain an anti-coagulant protein that helps the fly complete its blood meal. This invention relates to the identification of LJL143, a salivary gland protein of *L. longipalpis,* as a specific inhibitor of coagulation factor Xa. LJLl43 is secreted in the saliva of *L. longipalpis* and exerts its effects by tightly binding the catalytic site of factor Xa. By directly binding the catalytic site, it is believed that the potent anti-coagulant activity of LJL143 will be accompanied by reduced side effects compared to anti-coagulant drugs that rely on activating serine proteases. LJL143 has a novel sequence with no reported homology in the gene bank, and is the first anti-coagulant factor identified in sand flies.

LJLl43 may be used for inhibiting factor Xa activity *in vivo* or as a prototype for designing specific inhibitors of factor Xa. Because of its high specificity, LJLl43 may be used as an anti-coagulant in a number of pro-coagulant diseased states including deep venous thrombosis, coronary artery disease, non-hemorrhagic stroke, and unstable angina with potentially reduced side effects.

Applications:

• Safe and effective anti-coagulant for therapeutic use.

• Treatment of several conditions such as deep venous thrombosis, coronary artery disease, non-hemorrhagic stroke, and unstable angina.

Advantages: May be safer than other important blood thinning drugs such as Warfarin.

Development Status: Early Stage.

Market: Predicted $7.4 billion anti-coagulant market by 2016.

Inventors: Jesus G. Valenzuela *et al.* (NIAID).

Publication: JG Valenzuela, M Garfield, ED Rowton, VM Pham. Identification of the most abundant secreted proteins from the salivary glands of the sand fly *Lutzomyia longipalpis,* vector of *Leishmania chagasi.* J Exp Biol. 2004 Oct;207(Pt 21):3717–3729.

Patent Status: U.S. Provisional Application No. 61/142,107 filed 31 Dec 2008 (HHS Reference No. E–204–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Jeffrey A. James, PhD; 301–435–5474; *jeffreyja@mail.nih.gov.*

Novel Dopamine Receptor Ligands as Therapeutics for Central Nervous System Disorders

Description of Technology: The dopamine D3 receptor subtype is a member of the dopamine D2 subclass of receptors. These receptors have been

implicated in a number of CNS disorders, including psychostimulant abuse, psychosis and Parkinson's disease. Compounds that bind with high affinity and selectivity to D3 receptors can not only provide important tools with which to study the structure and function of this receptor subtype, but may also have therapeutic potential in the treatment of numerous psychiatric and neurologic disorders.

The 4-phenylpiperazine derivatives are an important class of dopamine D3 selective ligands. However, due to their highly lipophilic nature, these compounds suffer from solubility problems in aqueous media and reduced bioavailability. To address this problem, a process was designed to introduce functionality into the carbon chain linker of these compounds. Compared to currently available dopamine D3 receptor ligands, the resulting compounds show improved pharmacological properties and D3 selectivities but due to their more hydrophilic nature, these derivatives are predicted to have improved water solubility and bioavailability.

Applications:

• Therapeutics for a variety of psychiatric and neurologic disorders

• Research tools to study D3 receptor structure and function

Advantages:

• Improved pharmacological properties and selectivity over existing dopamine D3 receptor ligands

• Hydrophilic nature likely to lead to improved water solubility and bioavailability

Development Status: Pre-clinical discovery.

Further R&D Needed:

• Evaluate selected compounds in animal models of drug abuse, psychosis, obesity and Parkinson's disease.

• Design and synthesize novel, functionalized analogs using both classical and computational drug design to improve D3 receptor affinity and selectivity.

• Evaluate compounds for binding in D3 and D2 receptor expressing cell lines and in in vitro functional assays.

• Correlate in vitro binding affinities with in vivo function in rats and monkeys and evaluate compounds in knockout mice models.

• Pursue PET and SPECT imaging agents by radiolabel of D3 ligands and evaluation in rats and non-human primates.

Inventors: Amy H. Newman (NIDA), Peter Grundt (NIDA), Jianjing Cao (NIDA), *et al.*

Patent Status: PCT Application No. Pct/US2007/71412 filed 15 Jun 2007, which published as WO 2008/153573 on 18 Dec 2008 (HHS Reference No. E–128–2006/0–PCT–01).

Licensing Status: Available for licensing.

Licensing Contact: Charlene Sydnor, PhD; 301–435–4689; *sydnorc@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute on Drug Abuse's Medications Discovery Research Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize 4-phenylpiperazine derivatives as dopamine D3 selective ligands. Please contact Vio Conley, MS at 301–435–2031 or *conleyv@mail.nih.gov* for additional information.

High-Yield Methods of Producing Biliverdin

Description of the Technology: This invention describes methods of making high yields of biliverdin, the pharmaceutical compositions of biliverdin made using that process, and methods of using the compositions therapeutically.

In reaction to a wide range of cellular stresses, hemoglobin is naturally metabolized to biliverdin, which is then quickly metabolized to bilirubin, a bile pigment, through a highly conserved set of enzymes. Both bilirubin and biliverdin are normally processed for rapid excretion, and excessive serum levels of bilirubin have known toxic effects (most notably jaundice). Surprisingly, research in the past decade has shown that decreasing serum levels correlate *inversely* with the prognosis of various disorders, such as ischemia/reperfusion injuries, atherosclerosis, organ transplantation, and several autoimmune diseases. Indeed, in animal-model studies, inducing a mild case of jaundice actually improved outcome. Unfortunately, bilirubin is relatively insoluble, and so is not a practical pharmaceutical itself.

Biliverdin has lower direct toxicity and substantially greater solubility than bilirubin, and also appears to have some direct therapeutic effects similar to bilirubin. Accordingly, biliverdin has been widely studied lately. Generating high yields of pure biliverdin is difficult, however, because any system with the enzymes to break down hemoglobin also has enzymes converting biliverdin to bilirubin. The inventors have created a system of generating microorganisms (yeast) lacking the enzymes that break biliverdin down to bilirubin.

Applications: Production of biliverdin for immunomodulatory and cytoprotective therapy (or adjuvant) in any condition involving an overactive immune response.

Advantages:

• High yield of biliverdin with low contamination of bilirubin.

• Produces only active isomers of biliverdin.

• Unlike prior methods, new method uses starting material that is inexpensive and plentiful.

Development Status: Successful generation of *Candida albicans* with biliverdin-generating system.

Inventors: Michael L. Pendrak and David D. Roberts (NCI).

Patent Status: HHS Reference No. E–040–2004/0—Issued U.S. Patent 7,504,243; Pending U.S. Application 12/364,054 (divisional, filed 02 Feb 2009).

Relevant Publication: ML Pendrak *et al.* Heme oxygenase in Candida albicans is regulated by hemoglobin and is necessary for metabolism of exogenous heme and hemoglobin to alpha-biliverdin. J Biol Chem. 20 Jan 2004;279(5):3426–3433.

Licensing Status: Available for licensing.

Licensing Contact: Bruce Goldstein, JD, MS; (301) 435–5470; *goldsteb@mail.nih.gov.*

Collaborative Research Opportunity: The Laboratory of Pathology in the Center for Cancer Research of the National Cancer Institute is seeking parties interested in collaborative research directed toward clinical applications of biliverdin. For more information about the research, please contact either Dr. Michael Pendrak (NCI/CCR Laboratory of Pathology) at (301) 496–6264, or Dr. April Franks (NCI Technology Transfer Center) at (301) 496–0477.

Dated: July 28, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–18496 Filed 7–31–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2009–N–0338]

Medical Device User Fee Rates for Fiscal Year 2010

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the