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.

Conditional Knockout of Smad1 in Mice

Description of Technology: NIH inventors have generated a conditional knockout of Smad1, a protein involved in the TGF-beta family signaling pathways. LoxP elements were made to flank exon 2 of Smad1 in one set of mice. These mice can be crossed with mice expressing the CRE element in a tissue-specific or inducible manner. These mice can be used to study the role of Smad1 under a variety of conditions in a variety of different paradigms.

Applications:
• Tool for studying role of Smad1 in development in general or in a specific tissue.
• Tool for studying the role of Smad1 in a tissue-specific and/or an inducible way.

Inventor: Dr. Shixia Huang (NCI).

Clk and Dyrk1A Inhibitors as General Splicing Modulators and for the Potential Treatment of Down’s Syndrome and Alzheimer’s Disease

Description of Technology: NIH investigators have discovered a series of potent, selective small molecule inhibitors of cdc2-like kinases (Clk) and dual-specificity tyrosine-regulated kinase 1A (Dyrk1A) with potential as modulators of gene splicing and within the treatment of Down’s syndrome and Alzheimer’s disease. Clk kinases are known to phosphorylate the prominent family of serine- and arginine-rich (SR) splicing proteins. Members of the Clk family have been implicated in the regulation of alternative splicing of PKCζII, TF, Tau and β-globin pre-mRNA. Dyrk1A is a kinase that has been implicated in numerous aspects of neurological development and maintenance. The gene that encodes Dyrk1A is found on the Down’s Syndrome-critical region on chromosome 21 and the over-expression of Dyrk1A is considered to be a primary contributor to the Down’s syndrome phenotype. For instance, transgenic mice overexpressing Dyrk1A exhibit cognitive deficits, and blocking Dyrk1A in these transgenic animals has been shown to mitigate Down’s-related deficits. Hyper-phosphorylation of Tau by Dyrk1A has also been directly implicated in the pathology and progression of Down’s syndrome-associated Alzheimer’s disease. Alzheimer’s disease in general is also associated with pathological deposition of hyper-phosphorylated Tau. Thus, these molecules have the potential to treat both Down’s syndrome and Alzheimer’s disease.

Applications:
• Tools for the study of alternate gene splicing.
• Potential therapeutic for Down’s syndrome.
• Potential therapeutic for Alzheimer’s disease.


Related Publication: S Kurebayashi, E Ueda, S Sakaue, DD Patel, A Medvedev, F Zhang, AM Jetten. Retinoid-related orphan receptor gamma (RORγ) is a member of the nuclear receptor superfamily. NIH investigators used homologous recombination in embryonic stem cells to generate mice in which the RORγ gene was disrupted. RORγ deficient mice lack peripheral and mesenteric lymph nodes and Peyer’s patches indicating that ROR expression is indispensable for lymph node organogenesis. In addition, RORγ is required for the generation of Th17 cells which play a critical role in autoimmune disease.

The RORγ deficient mice are useful to identify the physiological functions of the RORγ. RORγ deficient mice also provide an excellent tool to study the role of RORγ in immune responses and autoimmune disease, the study of the role of Th17 and interleukin 17 in these processes, and the analysis.

Inventor: Anton M. Jetten (NIEHS).

Licensing Status: Available for licensing under a Biological Materials License Agreement.
License Contact: Suryanarayana (Sury) Yapa, PhD, J.D.; 301–435–5020; vepas@mail.nih.gov.

Collaborative Research Opportunity: The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the ROR gamma mice or related laboratory research interests. Please contact Dr. Elizabeth Denholm at denholme@niehs.nih.gov or 919–541–0981 for more information.

Antibody Composition and Methods for the Prevention and Treatment of Lupus Nephritis

Description of Technology: This technology identifies an antibody that induces a protective effect in vivo in a mouse model of lupus nephritis. Lupus is a chronic autoimmune disease that can damage various parts of the body, especially the kidneys. The lupus nephritis-model mice that were treated with this antibody experienced a dramatic increase in survival, demonstrated a reduced immune complex deposition in the kidneys, and displayed low levels of proteinuria as compared with untreated mice. The antibody is an autospecific anti-dsDNA IgM.

In addition, this invention may be used as a component of a predictive diagnostic kit. As lupus-related kidney disease may be asymptomatic, significant kidney damage may occur before lupus is diagnosed (lupus.org). The inventors are currently investigating whether the ratio of protective antibodies to nonprotective or pathogenic antibodies in lupus nephritis models is predictive of disease. Currently available diagnostic methods (proteinuria, creatine clearance, or kidney biopsy) are not predictive and test only for existing kidney impairment or damage.

Applications:
• A preventative and therapeutic for lupus nephritis.
• A component of a predictive diagnostic kit for lupus nephritis.
• A research tool for investigation of lupus nephritis in a mouse model.

Advantages:
• Therapeutic antibodies are unlikely to elicit side effects in patient populations, unlike many existing therapies.
• The diagnostic would be predictive, unlike existing diagnostics.

Development Status: Early stage, in vivo (mouse).

Market:
• At least 1.5 million Americans have lupus (lupus.org).
• Up to 67% of children with lupus, and approximately 40% of all individuals with lupus, develop lupus-related kidney complications (lupus.org).

Inventors: Marilyn Diaz, Chuancang Jiang, Ming-Lang Zhao (NIEHS).

Publication: In preparation.


Licensing Status: Available for licensing.

Licensing Contact: Norbert Pontzer, J.D., PhD; 301–435–5502; pontzerN@nich.nih.gov.

Collaborative Research Opportunity: The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology or related laboratory research interests. Please contact Dr. Elizabeth Denholm at denholme@niehs.nih.gov or 919–541–0981 for more information.

P2Y<sub>1</sub> Receptor Antagonists Useful for the Study of Platelet Aggregation and Clotting Conditions

Description of Technology: NIH inventors have developed P2Y<sub>1</sub> receptor antagonists [(N)-Methanocarba 2′-Deoxyadenosine 3′, 5′-Bisphosphate Analogues] for inhibition of platelet aggregation and treatment of clotting conditions. On the platelet surface, simultaneous activation of the P2Y<sub>1</sub> and P2Y<sub>12</sub> receptors by ADP induces aggregation. The P2Y<sub>1</sub>-mediated response is associated with the initial shape change and rapid aggregation, and the P2Y<sub>12</sub> receptor is associated with amplification of the aggregation. P2Y<sub>12</sub> receptor antagonists are both in clinical use and under development as antithrombotic agents. Potent and selective P2Y<sub>1</sub> receptor antagonists, such as the conformationally locked methanocarba nucleotide MRS2500 1 (K, 0.79 nM), have been designed and shown to have promise in preclinical studies as antithrombotic agents. This novel drug concept is also supported by studies of mice in which the P2Y<sub>1</sub> receptor has been genetically deleted, wherein the initiation of clotting events is markedly impaired.

Applications: Potential new target for treating intravascular clotting.

Development Status: Early-stage of development.

Market: There is a very large potential market for P2Y<sub>1</sub> receptor antagonists. For instance, P2Y<sub>1</sub> receptor antagonists may treat deep vein thrombosis, which occurs in 80 of 100,000 individuals in the U.S. annually.

Inventors: Kenneth A. Jacobson and Sonia De Castro (NIDDK).

Patent Status:

Licensing Status: Available for licensing.

Licensing Contact: Steve Standley, PhD; 301–435–4074; sstand@od.nih.gov.


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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Medicare & Medicaid Services

[CMS–6023–CN]

Medicare Program; Solicitation of Independent Accrediting Organizations To Participate in the Advanced Diagnostic Imaging Supplier Accreditation Program; Correction

AGENCY: Centers for Medicare & Medicaid Services (CMS), HHS.

ACTION: Correction notice.

SUMMARY: This document corrects a technical error in the notice entitled “Medicare Program; Solicitation of Independent Accrediting Organizations to Participate in the Advanced Diagnostic Imaging Supplier Accreditation Program” which was posted for public inspection by the Office of the Federal Register on October 30, 2009, and published in the Federal Register on November 23, 2009.

FOR FURTHER INFORMATION CONTACT: Sandra Bastinelli, (410) 786–3630.

SUPPLEMENTARY INFORMATION:

I. Background

In FR Doc. E9–26209, which was posted for public inspection by the Office of the Federal Register (OFR) on October 30, 2009, and published in the Federal Register on November 23, 2009, we made a technical error that is corrected in the Correction of Errors section below. The provisions in this correction notice are effective as if they had been included in the November 25, 2009 notice.