MRI Contrast Agents Depending on Proton Chemical Exchange

Robert S. Balaban, Kathleen Ward, Anthony H. Aletras (NHLBI)

DHHS Reference No. E–240–98/0 filed 21 Apr 1999

Recently, methods have been developed to Magnetic Resonance Imaging (MRI) contrast using exogenous agents with exchangeable protons. These methods incorporate the use of selective reagents, such as sugars, amino acids, and nucleosides with appropriate proton exchange sites. Image contrast is generated by using saturation transfer techniques to selectively affect the water protons used in forming the MR image. The contrast agents developed do not contain metals or metal chelates. The agents have appropriate exchangeable proton sites which can be irradiated at known frequencies to obtain MRI images with specific contrast. This permits the image contrast to be turned off and on based on the irradiation scheme. This method also uses a controlled irradiation scheme to overcome the obstacle of broad proton resonance that limits contrast enhancement. In-Vivo data has shown the utility of this invention.

Oligomeric HIV–1 Envelope Glycoproteins

Patricia L. Earl, Chris C. Broder, Robert W. Doms, Bernard Moss (NIAID)

Serial Nos. 08/165,314 filed December 10, 1993; 08/805,889 filed March 3, 1997; 09/070,291 filed April 30, 1998; and 09/415,326 filed October 8, 1999

This invention embodies a method for generating antibodies to HIV–1 envelope glycoproteins, which could hold powerful implications toward both the diagnosis and the treatment of AIDS. Specifically, the method involves the expression of a soluble protein, gp140, and the generation of antibodies to this protein. gp140 is a recombinant version of gp160, a protein which normally is cleaved in vivo to generate two glycoprotein subunits which are expressed on the surface of the HIV–1 envelope. Unlike previously isolated versions of gp160, gp140 is purified in a manner which preserves the quaternary structural elements of the protein. Due to the conserved nature of these structural elements, antibodies generated against gp140 may be more broadly reactive against various forms of AIDS than other antibodies generated to date.

Dated: April 17, 2000.

Jack Spiegel,

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

[FR Doc. 00–10179 Filed 4–21–00; 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 agencies 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 contacting Susan S. Rucker, J.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7056 ext. 245; fax: 301/402–0220; e-mail: sr156v@nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Hybrid Adeno-Retroviral Vector for the Transformation of Cells

C Zheng, B O'Connell, BJ Baum (NIDCR)

Serial No. E–258–98/0 filed 31 Jan 2000

The invention described and claimed in this patent application provides for novel hybrid vectors which may be used for cell transformation, either in vivo or in vitro. The hybrid vectors have an adenoviral backbone with retroviral long terminal repeats (LTRs). Such vectors are capable of transforming dividing or non-dividing cells and integrate stably into the chromosome providing a means of efficient, reliable, long-term gene expression. The vector was packaged as a recombinant adenovirus and delivered to the target cell. Unlike other chimeric or hybrid vector systems, only a single vector is required to deliver a transgene of interest, and retroviral structural proteins are not required.

This work has been published in part in Nature Biotechnology Zheng, et al. 18(2): 176–180 (Feb 2000).

Calcium Channel Compositions and Methods of Use Thereof

MI Lerman (NCI) *et al.*

Serial No. 09/470,443 filed 22 Dec 1999 and 60/114,359 filed 30 Dec 1998 (now abandoned)

This invention described in this patent application relates to the identification, isolation and cloning of a three cDNAs identified during a search of the short arm of chromosome 3 for a tumor suppressor gene (TSG) associated with lung cancer. The cDNA's are alternative isoforms which encode a protein which functions as a subunit of L-type voltage-dependent calcium channel. Type L voltage-dependent calcium channels represent one of five families of calcium channels, L, R, P, N, Q, which have been identified. Type L voltage-dependent calcium channels are found in a wide variety of tissues including the brain, muscle and the endocrine system.

The gene has been mapped to the short arm of chromosome 3 at 3p21.3. The gene, which corresponds to this cDNA is an alpha2delta-2 (α2δ-2) subunit, and has been shown to be deleted in lung and breast cancer. The scientists have demonstrated that the expression of this calcium channel has been shut off in lung cancer cells and hypothesize that this may lead to a malignant phenotype. Other cancers which may be associated with this α2δ-2 subunit include cervical cancer and head and neck carcinoma. Other non-malignant diseases which may also be associated with this α2δ-2 subunit include CNS diseases and cardiovascular diseases.

Possible applications of this technology include its use in drug screening assays; its use as an early diagnostic marker and/or as a prognostic or treatment indicator; its use in gene therapy where defective cells would be reconstituted with the gene and as a therapeutic agent for clearing autoantibodies which develop toward the alpha2delta-2 subunit in the disease Lambert-Eton myasthenia syndrome.

Monoclonal Antibody Against Met Protein

G Vande Woude, M Oskarsson, J Resau, S Rulong, Y Chui (NCI–FCRDC)

Serial No. 60/168,835 filed 03 Dec 1999

The invention described in this application relates to the Hepatocyte Growth Factor/Scatter Factor/Tumor Cytotoxic Factor (HGF/SF/F–TCF)-met/Hepatocyte Growth Factor Receptor

(HGFr) pathway. In particular, the invention described in this application is a murine monoclonal antibody, designated D1, which specifically binds to an epitope in the extracellular domain of human HGFr/met. The monoclonal antibody can be used, for example, to visualize HGFr/met expression in paraffin-embedded tumor samples and in drug screening assays (competitive binding assays) for antagonists/agonists of HGFr/met.

Determination of AM Binding Proteins and the Association of Adrenomedullin (AM) Therewith

F Cuttitta (NCI), A Martinez (NCI), R Pio (NCI), TH Elasser (USDA–ARS)
Serial No. 60/153,397 filed 10 Sep 99

This application relates to isolation and identification of a polypeptide which binds to the hormone adrenomedullin designated adrenomedullin binding protein 1 (AMBP1). Adrenomedullin (AM), a peptide hormone, has been implicated in a variety of physiological functions including the regulation of insulin production, anti-microbial activity, mitogenesis and angiogenesis. The activities of AM are believed to be mediated by a variety of binding proteins in a manner similar to the way in which Insulin-like Growth Factor (IGF) is regulated. AMBP1 has been purified to homogeneity and its amino acid sequence determined.

The application is directed to methods of measuring AM levels in plasma based on the finding that AMBP1 binds in a specific and reversible competitive fashion with AM and methods of treating AM related disease by administering AMBP1. Other aspects of the invention are complexes of AM with AMBP1 and antibodies which specifically bind to an epitope by the complex of AM with AMBP1 as well as assays for detecting the complex of AM with AMBP1.

This work has been published in part in Elsasser TH, et al. Endocrinology 140(10):4908–11 (Oct. 1999).

In addition to being available for licensing the NIH is willing to consider interest from companies who are interested in pursuing commercialization opportunities through a Cooperative Research and Development Agreement (CRADA).

AAV5 Vector and Uses Thereof

JA Chiorini, RM Kotin (NHLBI)
Serial No. PCT/US99/11958 filed 28 May 1999 based on USSN 60/087,029 filed 28 May 1998

The invention described and claimed in this patent application provides for novel vectors and viral particles which comprise adeno-associated virus serotype 5 (AAV5). AAV5 is genetically distinct from others AAVs with respect to its capsid proteins, VP1, VP2, and VP3, which contributes to different tissue tropisms for AAV5. The ITR and Rep proteins of AAV5 are also distinct which results in a biochemically unique mechanism of replication compared to the other AAVs. This difference in replication activity contributes to the fact that AAV5 is only able to replicate and package AAV5 ITR containing DNA in contrast to AAV2 which is able to replicate and package other AAV serotypes. Vectors produced using AAV5 proteins may be useful in gene therapy.

AAV5 offers several advantages which make it attractive for use in gene therapy: (1) increased production (10–50 fold greater than AAV2); (2) its distinct replication mechanism when compared to AAV2; (3) its Rep protein and ITR regions which do not complement other serotypes; (4) it appears to utilize different cell surface attachment molecules than those of AAV type 2; and (5) improved efficiency of transduction of certain cell types including airway epithelial, striated muscle, endothelial, and neuronal cells when compared to AAV type 2.

This work has been published, in part, in J. Virol. 73(5): 4293–98 (May 1999) and J. Virol. 73(2): 1309–19 (Feb. 1999).

Prevention of Fetal Alcohol Syndrome and Neuronal Cell Death with ADNF Polypeptides

DE Brenneman (NICHD), CY Spong (NICHD), I Gozes (TAU), M Bassan (TAU), R Zamostiano (TAU)
Serial No. 09/267,511 filed 12 Mar 1999

This patent application describes an extension of prior work related to peptides derived from proteins known as ADNF and ADNF III/ADNP. These peptides are known as SAL (ADNF-derived) and NAP (ADNP-derived). SAL and NAP (L-isomers) have previously been demonstrated, in in vitro work, to be able to prevent neuronal cell death and to protect against the toxic activities of a cholinotoxin suggesting that they are useful as therapeutics for neurodegenerative diseases. The new work presented in this EIR demonstrates that NAP and SAL (L-isomers), alone or in combination, prevent damage to neurons due to oxidative stress. In particular, the new work shows that NAP and SAL (L-isomers) alone or together are effective in preventing damage due to oxidative stress in a model for fetal alcohol syndrome. Thus, NAP and SAL (L-isomers), alone or together may be useful therapeutically to treat fetal alcohol syndrome.

In addition, a number of other patent applications and patents related to this technology have been filed by PHS and are available for licensing. These include: USP 5,767,240 (PCT/US92/03109); 08/324,297 (PCT/US95/12929); 60/037,404 (PCT/US98/07485); 09/187,330 (PCT/US99/26213) 60/149,956; and 09/364,609.

Dated: April 18, 2000.

Jack Spiegel,

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

[FR Doc. 00–10180 Filed 4–21–00; 8:45 am]

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Identification of a Novel Amplified Gene, MB1, at 17q23

Anne H Kallioniemi, Maarit T Barlund, Outi M Monni, Juha T Kononen, Olli P Kallioniemi (NHGRI)
DHHS Reference No. E–038–00/0 filed 13 Dec 1999

DNA amplification at 17q23 is one of the most common genetic alterations in breast cancer. Genes affected by this amplification may have a critical role in