

analysis. This method has been used in *S. cerevisiae* for many yeast chromosomal genes and the human gene p53 and has obvious potential for use with YAC and TAR clones. Claims are directed to several methods for generating DNA nucleic acid mutations in vivo and are applicable to any organism that has a homologous recombination system, as well as to kits. This methodology is available for licensing and is a highly versatile tool of direct use to drug discovery, pharma and research reagent companies as well as to companies working with industrial yeast strains.

In addition to licensing, the technology is available for further development through collaborative research with the inventors via a Cooperative Research and Development Agreement (CRADA).

Related technologies also available for licensing include: DHHS Ref. No. E-121-1996/0-US-06, Transformation-Associated Recombination Cloning (U.S. Patent No. 6,391,642 issued 21 May 2002); and DHHS Ref. No. E-262-1984/0-US-03, Process for Site Specific Mutagenesis Without Phenotypic Selection (U.S. Patent No. 4,873,192 issued 10 Oct 1989).

#### **The Whey Acidic Protein (WAP) Promoter and Its Use to Express Therapeutic Proteins in the Milk of Transgenic Mammals**

Lothar Hennighausen (NIDDK), Heiner Westphal (NICHD), *et al.* U.S. Patent No. 6,727,405 issued 27 Apr 2004 (DHHS Reference No. E-411-1987/0-US-03).

*Licensing Contact:* Susan Carson; 301/435-5020; [carsonsu@mail.nih.gov](mailto:carsonsu@mail.nih.gov).

Transgenic animals can be engineered to express complex human proteins at high concentrations in milk. Protein replacement therapy is often the only treatment available for congenital diseases such as hemophilia or lysosomal storage disease, and the cost of treatment can be high with the therapeutic protein market estimated to reach more than \$50 billion by 2010.

U.S. Patent No. 6,727,405 has recently been issued (expiry date 2021) to NIH scientists and their collaborators. This patent provides for a non-human mammal such as mouse, sheep, pig, goat and cow whose genome contains a DNA sequence comprising a milk serum protein (whey acidic protein) promoter linked to a heterologous gene sequence and secretory peptide, as well as methods for producing a secreted protein into the transgenic animal's milk and claims directed to the DNA construct. The invention permits the production of any desired protein in an

easily maintained, stable, mammalian bioreactor, which is capable not only of producing the desired protein in milk, but can also pass the ability to do so to its female offspring. Although other methods of obtaining recombinant protein products are available, these require inefficient, expensive purification of the protein from the blood or from cell culture media and there remains a need for an efficient and cost effective method for producing therapeutic proteins.

This WAP promoter platform technology provides a viable alternative to other milk protein promoters and is available for non-exclusive licensing.

Dated: January 31, 2005.

**Steven M. Ferguson,**

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

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**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.

**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.

#### **A3 Adenosine Receptor Agonists**

Kenneth A. Jacobson *et al.* (NIDDK). U.S. Provisional Patent Application No. 60/608,823 filed 09 Sep 2004 (DHHS Reference No. E-248-2004/0-US-01).

*Licensing Contact:* Marlene Shinn-Astor; (301) 435-4426; [shinnm@mail.nih.gov](mailto:shinnm@mail.nih.gov).

Researchers have been pursuing compounds that activate or inhibit adenosine A3 receptors because these cell membrane proteins have a wide range of physiological and disease-related effects and are thus considered to be promising drug targets. The adenosine A3 receptors are G-protein-coupled receptors and are found mostly in brain, lung, liver, heart, kidney, and testis. When this receptor is activated moderately, a cytoprotective effect is observed, such as reducing damage to heart cells from lack of oxygen. However, at high levels of stimulation they can cause cell death. Both agonists and antagonists are being tested for therapeutic potential, for example, treatment of cancer, heart conditions, neurological conditions, pain, asthma, inflammation and other immune implications.

Adenosine receptors have provided fertile leads for pharmaceutical development, and there are currently a variety of adenosinergic compounds advancing toward clinical trials. Therapeutics which target the adenosine A3 receptors is now an emerging focus that the major pharmaceutical companies are developing. Smaller companies are also developing drugs that stem from proprietary technology targeting adenosine A3 receptors. These companies have products in clinical trials for colorectal cancer and rheumatoid arthritis.

This invention pertains to highly potent A3 adenosine receptor agonists, pharmaceutical compositions comprising such nucleosides, and a method of use of these nucleosides.

This research has been published, in part, in S. Tchilibon, B.V. Joshi, S.-K. Kim, H.T. Duong, Z.-G. Gao, and K.A. Jacobson, "N-methano adenosine derivatives as A3 receptor agonists," *J. Med. Chem.*, ASAP web release date 23 Sep 2004, doi: 10.1021/jm049580r.

In addition to licensing, the technology is available for further development through collaborative research with the inventors via a Cooperative Research and Development Agreement (CRADA).

#### **Apparatus for Multifocal Deposition and Analysis**

Bradford Wood, Alexander Gorbach, Ziv Neeman, Julia Hvisda (all of NIHCC), *et al.* U.S. Provisional Patent Application No. 60/403,875 filed 16 Aug 2002 (DHHS Reference No. E-248-2001/0-US-01); International Application Number PCT/US03/25575 filed 14 Aug 2003, which

published as WO 2004/016155 A3 on 26 Feb 2004 (DHHS Reference No. E-248-2001/0-PCT-02).

Licensing Contact: Michael Shmilovich; (301) 435-5019; [shmilovm@mail.nih.gov](mailto:shmilovm@mail.nih.gov).

Available for licensing and commercial development is a multifocal apparatus for delivering an agent or for gathering information about a biological tissue, such as optical spectroscopy for tissue characterization (nuclear chromatic density). The apparatus includes a needle or catheter having a

lumen extending longitudinally at least partially through it and a deployment port within the distal portion of the catheter. A plurality of extendable-retractable needles are housed within the catheter lumen, when deployed, extend through the deployment port. The needles may be solid or hollow and may deliver an agent to the tissue, include a mechanism for gathering information about the tissue, or both. Optical spectroscopy in a needle-based system provides in vivo tissue characterization without removal of

tissue for microscopic analysis, which may be helpful during surgery or image guided therapies to localize cancerous tissue.

Figure 1 is a schematic diagram of one embodiment of the apparatus in use. The distal end of the apparatus is shown within a neoplasm and the needles are in a deployed state.

Figure 2 is an enlarged, longitudinal section through the distal end of an embodiment of the apparatus, showing several extendable-retractable needles in a non-deployed, or retracted, state.

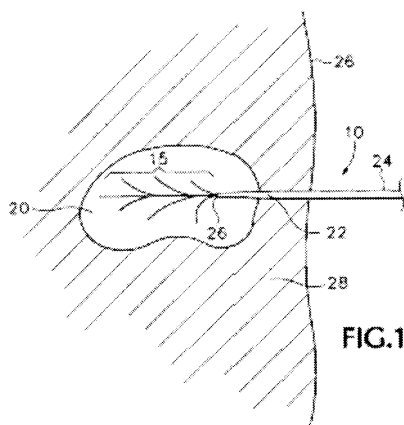


FIG.1

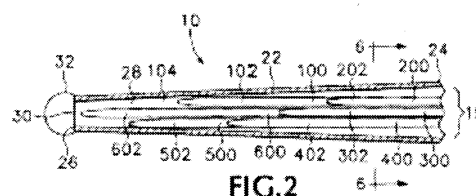


FIG.2

In addition to licensing, the technology is available for further development through collaborative research with the inventors via a Cooperative Research and Development Agreement (CRADA).

Dated: February 1, 2005.

**Steven M. Ferguson,**

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

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#### Monoclonal Antibody 90.12 Recognizes a Novel B Cell Surface Antigen Upregulated on Both Activated and Apoptotic Lymphocytes

Marjorie A. Shapiro *et al.* (FDA). DHHS Reference No. E-195-2004/0—Research Tool.

Licensing Contact: Cristina Thalhammer-Reyero; 301/435-4507; [thalhamc@mail.nih.gov](mailto:thalhamc@mail.nih.gov).

Monoclonal antibody 90.12 recognizes a molecule expressed on the surface of a subset of B lymphocytes and on all types of blood cells. This antigen is increased upon stimulation of B and T lymphocytes as well as on cells undergoing programmed cell death.

Amino acid sequencing of the beginning of the protein suggests that it is a member of the S100 family of calcium binding proteins. The antibody is further described in "Characterization of a B cell surface antigen with homology to the S100 protein MRP8" by Shapiro MA, Fitzsimmons SP, Clark KJ, Biochem Biophys Res Commun. 1999 Sep 16;263(1):17-22 and "A novel activation induced lymphocyte surface antigen, 90.12, is also expressed on apoptotic cells" by Clark KJ, Monser M, Stein KE, Shapiro MA, Scand J Immunol. 2000 Feb;51(2):155-63.

#### Methods for Analyzing High Dimensional Data for Classifying, Diagnosing, Prognosticating, and/or Predicting Diseases and Other Biological States

Javed Khan and Paul S. Meltzer (NHGRI), *et al.*

U.S. Patent Application No. 10/133,937 filed 25 Apr 2002 (DHHS Reference No. E-324-2001/0-US-01).

Licensing Contact: Cristina Thalhammer-Reyero; 301/435-4507; [thalhamc@mail.nih.gov](mailto:thalhamc@mail.nih.gov).

This invention relates to a method of using supervised pattern recognition methods to classifying, diagnosing, predicting, or prognosticating various diseases. The method includes