cycle components, oncogenes, tumor suppressor genes, DNA repair genes, estrogen-responsive genes, oxidative stress genes, and genes known to be involved in apoptotic cell death. This technology is in developmental stages at NIEHS, and we are interested in establishing relationships with CRADA partners to further our efforts on technology development and application toward toxicology research.

NIEHS seeks partnerships for collaboration in the development of arrayed cDNA libraries from various tissue sources, the development of toxicology models to test/validate the use of microarray technology in toxicology testing, and the development of bioinformatics support involving pattern recognition and classification.

Roles of NIEHS

1. Provide project coordination for overall project development and testing.
2. Establish various classes of toxicology gene expression arrays and subarrays based on existing data from toxicology studies or specific cDNA libraries.
3. To manufacture DNA chips from provided DNA sets and arrayed libraries, label and hybridize RNA probes to the expression arrays, and scan data and analyze and compile results.
4. To validate methods and expression array patterns using probes generated from established toxicology exposure models that have been developed by NIEHS or CRADA partner(s).

Role of the CRADA Partner(s)

1. Provide cDNA libraries from rodent and human sources that may be compatible for use to generate targets for use in synthesis of gene chips. May include custom cDNA library isolation from a variety of species and tissue sources.
2. Provide clone arrays from cDNA libraries from rodent and human sources, including arrays from custom, tissue-specific cDNA libraries. Also includes the sequence validation of arrayed clones.
3. Provide RNAs from traditional toxicology assays/models for use in validation testing of the use of microarray in toxicological identification/exposure assessment.
4. Provide bioinformatics/database support to subarray development and compilation and analysis of data, including pattern recognition from expression analyses experiments.

Selection criteria for choosing the CRADA partner(s) will include, but will not be limited to, the following:

1. Experience in the generation of high quality cDNA libraries, including custom and subtractive libraries. Ability to array cDNA libraries and provide resources to sequence-validate library clones.
2. Experience in toxicology testing models and ability to provide high quality and quantity RNA from these models.
3. Experience in database management and the development of software for the analysis of pattern recognition. May also include plasmid purification and PCR amplification of DNA from existing sub-arrayed library sets.

Dated: February 1, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–3237 Filed 2–9–99; 8:45 am]

BILLING CODE 4140–01–M

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 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 Method Of Using A β_2-Adrenergic Receptor Agonist That Selectively Activates G_s Proteins In The Treatment Of Cardiovascular Disease

Rui-Ping Xiao, Edward G Lakatta, Heping Cheng (NIA)
Serial No. 60/102,475 filed 30 Sep 98
Licensing Contact: Charles Maynard; 301/406–7735 ext. 243; *e-mail:* cm251n@nih.gov

This technology relates to a method of using β_2-adrenergic receptor agonist that selectively activates G_s proteins in the treatment of cardiovascular disease. In particular, this invention relates to a method of using fenoterol to activate selectively G_s proteins in the treatment of acute heart failure, chronic heart failure and aging heart. In the heart, β-adrenergic receptor (βAR) stimulation provides the primary regulatory mechanism on cardiac function. There are at least two βAR subtypes, namely β_1AR and β_2AR, that exist in the myocardium, although β_1AR predominates. While β_1AR couples to stimulatory G proteins (G_s), β_2AR elicits bifurcated signaling pathways mediated by G_s and G_i, resulting in functionally opposing effects on cardiac function. In failing and aged hearts, the overall response to βAR stimulation is markedly diminished due to the down-regulation of β_1AR and an up-regulation of G_i proteins.

This invention is predicated on the surprising and unexpected discovery that a β_2AR agonist can selectively activate G_s proteins, and is further predicated on the discovery that selective activation of G_s proteins by a β_2AR agonist can revive βAR contractile support in failing hearts.

An object of the present invention is to provide ligands (agonists and antagonists), and methods for the selective activation and inactivation of a subset of signaling pathways coupled to any given receptor of any cell or tissue type. It is another object of the present invention to provide ligands and methods for the selective activation and inactivation of a subset of signaling pathways involving G proteins. In particular, G_s and G_i proteins coupled to a cardiovascular receptor such as β_2 AR for the treatment of cardiovascular disease.

Aminohydroxylated Adenine Derivatives

KB Sharpless, DM Jerina, KR Dress, LJ Goossen, AS Pilcher, H Kroth, AR Ramesha (NIDDK)
Serial No. 60/091,900 filed 07 Jul 98
Licensing Contact: Charles Maynard; 301/496–7735 ext. 243; *e-mail:* cm251n@nih.gov

The invention herein describes a process for the addition of adenine and its derivatives to olefins to produce cis-vicinal aminoalcohols. The adenine moiety is contained in numerous drugs as well as plant growth regulators. In addition, adducts of purine bases in

DNA have been implicated in the transformation of normal cells to tumor cells. A key feature of the synthesis is that it provides a one-step high yield process for the production of adducts derived from the cis-opening of diol epoxide metabolites from polycyclic aromatic hydrocarbons. Previously such cis-opened adducts have not been readily accessible.

This technology provides compositions and synthetic methods for the preparation of important biologically active compounds. Typically, admixing adenine, olefin and ligand in the absence of oxygen with an appropriate catalyst produces the desired product for a wide range of substituted olefins and amino derivatives.

Mammalian Gene Insertion Libraries

X Zheng, CL Steward, SH Hughes, EV Barsov (NCI)
Serial No. 09/069,127 filed 28 Apr 98
Licensing Contact: Richard Rodriguez; 301/496–7056 ext. 287; *e-mail;* rr154z@nih.gov

Sequencing of the genomes of higher organisms is progressing rapidly, but only a fraction of the open reading frames and cDNAs whose sequence are known have functions associated with them. There is therefore a great need to assign functions to these open reading frames. One method of achieving this goal is insertional mutagenesis using transposable elements. An insertion into a gene not only alters the structure of the gene but also serves as a molecular marker for characterizing and cloning the targeted gene. While effective, this approach has been problematic in mammals due to the large size and complexity of mammalian genomes and the lack of appropriate mammalian transposable elements. The current invention provides a mammalian insertional mutation library in which each cell has one or more copies of a vector inserted into its genome at essentially random locations, and the library as a whole includes insertions in the majority of the genes of the genome. The cells used to create the libraries can be of a variety of types, including totipotent cells, and can be used to generate a whole animal. The unique vectors used to make the libraries are retrovirus-based, replication-deficient in mammalian cells and are efficiently produced in avian cells at high titers. This technology allows for the efficient creation of transgenic mice in which a detailed investigation of the cellular processes that are affected by the expression of mutated gene sequences can be performed as well as an analysis of the consequences on the physiology of the whole animal.

Preparation of Chiral 5-Aminocarbonyl-5H-Dibenzo[A,D]Cyclohepten-5,10-Imines by Optical Resolution

TH Jones, Kc Rice (NIDDK)
Serial No. 08/420,013 filed 11 Apr 95; U.S. Patent No. 5,686,414 issued 11 Nov 97
Licensing Contact: Leopold Luberecki, Jr.; 301/496–7735 ext. 223; e-mail: 1187a@nih.gov.

This case discloses a means for chiral separation of 5-Aminocarbonyl-5H-Dibenz0[A,D] Cyclohepten-5,10-Imines (ADCI), a compound under development by an exclusive licensee as a treatment for epilepsy and nervous system disorders. Approximately one percent of the American population suffers from epilepsy or related seizure disorders, and many of these patients do not respond to currently available antiseizure medications. It can be assumed that if one of the enantiomeric forms of ADCI is more active than the other, the U.S. Food and Drug Administration and its equivalent foreign counterparts will require use of that stereoisomeric form of the compound.

A Novel Mouse Model For Non-Insulin Dependent (TYPE II) Diabetes Mellitus

CR Kahn, JC Bruening, D Accili (NICHD)
DHHS Reference No. E–123–96/0 filed 07 Jun 96
Licensing Contact: Charles Maynard; 301/496–7735 ext. 243;
e-mail: cm251n@nih.gov.

This technology relates to animal models of polygenic insulin-related disorders and methods of using such animals. The invention features a ''genetically engineered'' non-human animal having a first and second mutation in genes important for insulin action. The double ''knockout'' animal is useful as a model of polygenic insulin-related disorders, e.g., type II diabetes. Non-insulin dependent (TYPE II) diabetes mellitus (NIDDM) is among the most common of all metabolic disorders, affecting 6–7% of the U.S. population. Currently no good animal models exist for NIDDM. The most frequently used models are models of genetic obesity. In these obesity models, there is gradual development of insulin resistance as the obesity increases. The Goto-Kitazak (GK) rat has been proposed as a non-obese model of NIDDM, although the diabetes in this case is quite mild and the pathogenesis is much less well understood. Thus, a need still exists to develop a novel mouse model that closely resembles human NIDDM disease.

Dated: February 1, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–3238 Filed 2–9–99; 8:45 am]
BILLING CODE 4140–01–M

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.

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A General Strategy And Specific Software For Maintaining Knowledgebases Consisting Of Diverse Categories

S Shaw (NCI)
DHHS Reference No. E–260–98/0 filed 30 Nov 98

The present disclosure describes a data management system and process for efficiently storing and retrieving data on a computer. This invention is designed to combine maximum data management flexibility and stability into a unified knowledgebase applications; as a result it has diverse functionality which can replace users' fragmented world of specialized applications such as contact manager, administrative database, bookmark keeper, fact finder. Some unique features of this software-based invention