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 John Fahner-Vihtelic, Technology Licensing Specialist/Patent Advisor, at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7735 ext. 270; fax: 301/402–0220; e-mail: jf36z@nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Molecular Rotation Engine

Thomas D. Schneider (NCI)

DHHS Reference No. E–018–99/0 filed 03 Aug 1999

The present application describes a molecular-based macroscopic rotating engine. The engine is constructed of two cylinders, one inner and one outer whose inner surfaces are coated with oriented mobility or contractile proteins. In the presence to ATP the cylinders rotate relative to each other. Speed of relative rotation is controlled by the concentration of ATP or by nesting a series of cylinders inside each other. Power is controlled by adjusting the length of the cylinders. One advantage of this technology over other macroscopic motors is that it can be used to supply power to prosthetic implants and medical devices without the drawbacks associated with conventional power sources. Other advantages are that the motor operates at room temperature, fuels can be prepared by growing sugar so the motor does not contribute to carbon dioxide pollution and the waste products are biologically safe.

Layered Electrophoresis Scan: A Method for High Throughput Molecular Fingerprinting of Tissue and Cell Samples

Michael Emmert-Buck (NCI)

DHHS Reference No. E–079–99/0 filed 26 Jul 1999

Layered expression scanning is a technique which combines tissue and/or cell samples with a high-throughput array approach to provide a simple and rapid method for comprehensive molecular analysis. The method works by placing a biological sample (tissue section, or dissected cell populations, or lysates from cells) adjacent to a set of capture layers, each containing an individual hybridization molecule (antibody or DNA sequence). The specimen(s) is transferred through the membranes and, importantly, the overall two-dimensional architecture and histological relationships within the sample(s) are maintained. As the proteins and nucleic acids are transferred each target molecule specifically hybridizes to the membrane containing its antibody or complementary DNA sequence. After hybridization each of the membranes are analyzed, providing a measurement of the level of expression of each targeted molecule in all of the cell types present in the sample.

A Single Tube Homogeneous Assay for Lipoprotein Subfraction Analysis

Alan T. Remaley, Maureen Sampson, Gyorgy Csako (CC)

Serial No. 60/136,709 filed 28 May 1999

The present invention describes a single tube assay for determining high density lipoprotein HDL-cholesterol (HDL–C) and low density lipoprotein (LDL-–C) and total cholesterol (total–C), from a single serum sample. This technology is useful in determining a patient's risk factor for heart disease. Previously, multiple costly tests were performed in order to determine low density lipoprotein LDL–C and HDL–C by measuring total–C, total triglyceride, and HDL–C. That method of testing had limitations and was complex. In this methodology, the use of the homogeneous assay for HDL–C, does not require the physical separation of HDL. The new assay developed is efficient, less costly, and compares favorably to current assays for HDL–C, total cholesterol, and triglyceride. This technology may also be used to simplify the procedure for the point of care testing of hyperlipidemia.

Methods and Devices for Isolation and Analysis of Cellular Protein Content

Lance A. Liotta, Emmanuel P. Petricoin, Nicole Simone, Michael E. Buck (NCI)

Serial No. 60/120,288 filed 16 Feb 1999

The present provisional application presents a comprehensive method to determine protein characteristics of a sample tissue cell in order to quantitatively discern and compare the protein content of healthy cells versus diseased cells. Furthermore, the tissue source of a tumor metastasis is available from the acquisition of this information. The realms for molecular biology study are moving from genomics to proteomics, the study of variations in the protein levels of cells, caused by the state of the cell itself, whether healthy or unhealthy. The invention at hand provides a method for using new and innovative methods for superior cell analysis. Previous methods, such as UV-laser ablation of unwanted tissue regions and oil well isolation of tissue cells, were complex, labor intensive, and did not utilize the important protein stabilizers. Direct comparisons between healthy cells and tumor cells were not made due to limitations of the methods. The new method consists of first using the new method of Laser Capture Microdissection (LCM) to obtain pure cell populations. Next, the sample is placed in a device so that the proteins are solubilized. Now the immunological and biochemical methods and subsequent analyses are performed. These techniques include (but are not limited to) immunoassays, 1D and 2D gel electrophoresis characterization, Western blotting, Matrix Assisted Laser Desorption Ionization/Time of Flight (MALDI/TOF) and Surface Enhanced Laser Desorption Ionization Spectroscopy (SELDI). The methods listed above allow for the direct comparison of both qualitative and quantitative tissue content of healthy and diseased cells, from the same sample. The sequential method of using LCM, protein isolation, analysis and comparison is superior since by simply using immunohistochemistry, the location of the tumor is found, but none of the protein characteristics, such as amino acid sequence and binding ability are discerned as they are in the present application. In addition, by using protein fingerprinting, the source of the tumor metastasis is found effectively. The methodology at hand has been tested extensively with the different methods listed above. This technology can be used in hospitals and research pathology labs for quantitative measure of protein characteristics of cells.

Dated: September 7, 1999.

Jack Spiegel,

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

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Methods for Treating Tumors Using Anti-Angiogenic Compounds

Steven K. Libutti, Andrew L. Feldman (NCI), Serial No. 60/133,243 filed 07 May 1999.

Angiogenesis is the process of tumor vascularization which involves both positive and negative regulators. It is recognized as a critical process in tumor progression and is essential for the growth and persistence of solid tumors and their metastases. This vacularization is induced by a variety of pro-angiogenic factors, which are balanced against naturally occurring negative regulators of angiogenesis, such as endostatin.

Endostatin is a protein derived from the cleavage of the precursor collagen XVIII. It is an endogenous inhibitor of angiogenesis and tumor growth that can inhibit angiogenesis and can induce dormancy or regression of large tumors in mice. Furthermore, endostatin does not induce acquired drug resistance, a problem associated with chemotherapy and other cytochemical therapies. However, difficulties in producing sufficient recombinant endostatin for widespread clinical use has presented significant obstacles in developing an endostatin therapy model.

The present invention describes a method of delivering endostatin as well as other inhibitors of angiogenesis by administering an adenovirus vector carrying a modified endostatin gene. This method allows the host to produce high levels of secreted endostatin systemically and in the local tumor environment.

This invention obviates the need to systemically administer recombinant protein and may allow for more efficient treatment strategies.

Methods for Identifying Modulators of GADD45 Polypeptide Activity

Xin Wei Wang, Curtis C. Harris, Albert J. Fornace Jr., Jill D. Coursen. Qimin Zhan (NCI), Serial No. 60/126,069 filed 25 Mar 1999.

A common method of treatment for cancer is to give radiation or chemicals to damage cancer cell's DNA so badly that the cell dies. However, these treatments are equally toxic to healthy cells. One approach to protecting normal cells from exposure to anti-cancer treatments would be to simultaneously treat the cells with a second agent which interacts preferentially with the cancer cells making them more susceptible to toxic radiation or chemical effective. This could be achieved by ''sensitizing'' the cancer to toxic treatments so the growing tumor cells die with a smaller amount of toxic radiation or chemical.

This invention describes a method of ''sensitizing'' the DNA of a cancer cell making it more susceptible to conventional therapies including radiation. Utilizing this technology, patients could be exposed to radiation doses that would inactivate the cancer cell but spare the healthy cells. Normally, a cell with unrepaired DNA damage will die by apoptosis as it progresses part G2/M into mitosis. If the cell can ''stall'' its cell cycle long enough to repair this DNA damage, the self-destructive reaction may be avoided. However, if this stalling mechanism can be disturbed, less DNA repair time is available and thus relatively lesser amounts of anti-cancer agent are needed to kill the cell.

One possible mediator of this stalling mechanism is GADD45, a ubiquitously expressed polypeptide induced by irradiation or DNA damaging agents. Inhibiting GADD45 prevents the cell from sufficiently repairing DNA damage to prevent its self-destructive passage to apoptosis. Thus, when a GADD45 inhibitor is co-administered with a DNA damaging drug, the cell is more sensitive to the irradiation or damaging drug.

The present invention describes ingenious methods that have been embodied in a variety of ways so that, for the first time, GADD45 can be envisioned as a platform from which a variety of therapeutic interventions might be envisioned. These include but are not limited to, novel methods to assay for modulators of GADD45 as means to sensitize a proliferating cell to a DNA damaging agent by administration of novel inhibitors of GADD45 polypeptide activity.

Method for Detecting Radiation Exposure

Albert J Fornace, Jr. (NCI), Sally A. Amundson (NCI), Jeffrey Trent (NHGRI), Serial No. 60/121,756 filed 26 Feb 1999.

Ionizing radiation has many medical, industrial and military uses. Ionizing radiation is often used in the therapy of diseases such as cancer, however, exposure to biologically significant levels of such radiation can also cause genotoxic stress. In addition, many individuals are potentially exposed to radiation through occupational or accidental exposure. Such radiation can elicit a variety of cellular responses, ranging from cell-cycle arrest to mutation, malignant transformation, or cell death. The present invention describes a method for detecting exposure of organisms to biologically significant or hazardous amounts of ionizing radiation.

This invention describes the identification of a large set of genes that are induced by ionizing radiation. Different patterns of gene induction are produced depending upon dose of radiation and time after treatment. Many of these genes are induced by physiological doses of radiation routinely used for cancer therapy. These genes sets may be useful as markers of exposure to hazardous radiation, or as markers to predict the likely response of a particular tumor to radiation therapy, and subsequently to track and access the response of patients to radiotherapy. In addition, these gene sets may also be useful in toxicological and epidemiological research and studies.