final design, but the primary criterion for selecting potential Collaborator(s) is the scientific merit of proposals for developing a plan to identify novel candidate genes for obesity and insulin resistance using global gene expression profiling.

The control of clinical trials shall reside entirely with the Institute and the scientific participants of the trial. In the event that any adverse effects are encountered which, for legal or ethical reasons, may require communication with the FDA, the relevant collaborating institutions will be notified. Neither the conduct of the trial nor the results should be represented as an NIDDK endorsement of the drug under study.

DATES: Only written CRADA capability statements received by the NIDDK on or before May 1, 2001 will be considered during the initial design phase, confidential information must be clearly labeled. Potential Collaborators may be invited to meet with the Selection Committee at the Collaborator's expense to provide additional information. The Institute may issue an additional notice of CRADA opportunity during the design phase if circumstances change or if the design alters substantially.

FOR FURTHER INFORMATION CONTACT: Capability statements should be submitted to Dr. Michael W. Edwards, Office of Technology Development, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, BSA Building, Suite 350 MSC 2690, 9190 Rockville Pike, Bethesda, MD 20814–3800; Tel: 301/496–7778, Fax: 301/402–0535; Email: me1s@nih.gov.

SUPPLEMENTARY INFORMATION: Substantial evidence indicates that susceptibility to type 2 diabetes is largely genetically determined, especially in certain ethnic groups in which the prevalence of diabetes may be 10 times that of the general U.S. population. NIDDK has performed genomic linkage scans in subject populations and are planning to positionally clone diabetes susceptibility genes. In general, diabetes is not inherited as a simple Mendelian trait. Multiple genes with small to moderate effects are likely to contribute to the development of the diabetes. In most populations, obesity and insulin resistance precede and predict the development of type 2 diabetes. These traits are themselves highly heritable, suggesting that they have a substantial genetic basis. Genes influencing these metabolic precursors of type 2 diabetes may be fewer in number and, therefore, easier to identify than those contributing to the overall syndrome. An extensive study in the subject population has indicated several chromosomal regions that provide evidence for linkage not only to diabetes but also to pre-diabetic phenotypes. We plan to perform gene expression profiling experiments to identify susceptibility genes for obesity and insulin resistance that may serve as possible targets of intervention.

Capability Statements

A Selection Committee will utilize the information provided in the ''Collaborator Capability Statements'' received in response to this announcement to help in its deliberations. It is the intention of the NIDDK that all qualified Collaborators have the opportunity to provide information to the Selection Committee through their capability statements. The Capability Statement should not exceed 10 pages and should address the following selection criteria:

(1) The statement should provide specific details of the method to be utilized in the development of novel candidate genes for obesity and insulin resistance using global gene expression profiling.

(2) The statement should include a detailed plan demonstrating the ability to provide sufficient capacity using global gene expression profiling.

(3) The statement may include outline outcome measures of interest to the Collaborator. The specifics of the proposed outcome measures and the proposed support should include but not be limited to the following: global gene expression profiling expertise, specific funding commitment to support the advancement of scientific research, personnel, services, facilities, equipment, or other resources that would contribute to the conduct of the commercial development.

(4) The statement must address willingness to promptly publish research results and ability to be bound by PHS intellectual property policies (see CRADA: http://ott.od.nih.gov/NewPages/crada.pdf).

Dated: March 23, 2001.

Jack Spiegel,

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

[FR Doc. 01–8085 Filed 4–2–01; 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.

Methods and Compositions for Analysis of M3 Muscarinic Acetylcholine Receptors

Jurgen Wess, Masahisa Yamada (NIDDK), DHHS Reference No. E–291–00/0 filed 30 Oct 2000, Licensing Contact: John Rambosek; 301/496–7056 ext. 270; e-mail: rambosej@od.nih.gov

This invention discloses transgenic mice that have the M3 Muscarinic Acetylcholine Receptor deleted by gene knockout technology. These mice were developed in order to better understand the physiological relevance of the M3 receptor. Unexpectedly, these knockout mice have a phenotype that includes significant reduction in food intake, weight loss, peripheral fat deposits, as well as very low serum leptin and insulin levels. It was also found that the M3 receptor is highly expressed in the hypothalamus, a region of the brain known to be critically involved in regulation of food uptake. The mice also show physiological changes (increased levels of hypothalmic agouti-related peptide mRNA and decreased expression of propiomelanocortin mRNA) consistent with those observed in fasted animals. However, the knockout mice also have changes

(reduced levels of melanin concentrating hypothalmic mRNA) inconsistent with fasted animals. These data point to the existence of a novel cholinergic pathway involving M3 cholinergic receptor mediated stimulation of food intake. This technology strongly suggests that agents which can specifically and selectively act as antagonists of the M3 subtype receptors may be useful in the treatment of obesity.

Methods for Preventing Strokes by Inducing Tolerance to E-selectin

John M. Hallenbeck, et al. (NINDS), Serial No. 60/206,693 filed 24 May 2000, Licensing Contact: Norbert Pontzer; 301/496–7736 ext. 284; e-mail: pontzern@od.nih.gov

This invention provides methods of treating or preventing brain damage in stroke through administration of E-selectin, an inducible adhesion molecule on endothelial cells. The expression of E-selectin is induced on human endothelium in response to activation by cytokines IL–1 and TNF. E-selectin mediates the adhesion of various leukocytes, including neutrophils, monocytes, eosinophils, natural killer cells, and a subset of T cells to activated endothelium. Activation of vascular endothelial cells by proinflammatory cytokines is believed to be involved in conversion of the luminal surface of endothelium from anticoagulant and anti-inflammatory to procoagulant and pro-inflammatory leading to thrombosis. Segmental vascular activation and thrombosis are involved in the development of strokes.

Recently, a new method and pharmaceutical formulation have been found that induce tolerance mucosally, such as by intranasal administration. The potential of mucosally administered antigens to inhibit immune responses in an antigen specific fashion has encouraged attempts to apply these routes to counteract immune dysfunctions such as allergies and in particular, autoimmune disease. Intranasal administration of E-selectin induces tolerance to E-selectin and leads to immune-deviation of a subset of lymphocytes such that they can suppress activation of vessel segments that are beginning to express E-selectin. Thus the ability of intranasal E-selectin treatment to decrease stroke lesions and delay the onset of stroke in stroke-prone spontaneously hypertensive rats suggests that the initial vessel activation and damage in stroke may be immunologically mediated. Production of immunosuppression via antigen-specific modulation of the immune response (mucosal tolerance) should have no systemic immunosuppressive effects.

Dated: March 23, 2001.

Jack Spiegel,

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

[FR Doc. 01–8086 Filed 4–2–01; 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 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.

Analogs of Thalidomide as Potential Angiogenesis Inhibitors

William Figg et. al. (NCI)
DHHS Reference No. E–282–00/0; filed 27 Feb 2001
Licensing Contact: Matthew Kiser; 301/496–7735 ext. 224; e-mail: kiserm@od.nih.gov

The present invention relates to anti-angiogenesis compositions and methods of using the same. In particular, thalidomide analogs that actively inhibit angiogenesis in humans and animals are claimed. The present methods provide for the inhibition of unwanted angiogenesis through the administration of a composition comprising an effective amount of an ''active'' thalidomide analog.

Angiogenesis is the formation of new blood vessels from pre-existing vessels, and it is a prominent feature in solid tumor formation and metastasis. For example, angiogenesis seems to play an important role in tumors such as prostate cancer, breast cancer, CNS glioma, and renal cancer, to name a few. Prevention of angiogenesis could halt the growth of these types of tumors and help prevent the resultant damage due to the presence of these tumors.

Recent studies have promoted thalidomide as a potential inhibitor of angiogenesis. The anti-angiogenic activity initially attributed to thalidomide is actually the resulting effects of compounds that are only present following metabolic activation, i.e. ''active'' thalidomide metabolites. Accordingly, there is a need for the isolation, identification and characterization of these thalidomide metabolites that exhibit superior anti-angiogenic properties. Furthermore, there is a need for purified thalidomide analogs that can mimic the effects of these metabolites.

A number of thalidomide metabolites having superior anti-angiogenic properties have now been isolated and identified. In addition, thalidomide analogs that mimic the effects of the ''active'' thalidomide (metabolites and variations of such thalidomide analogs) have been synthesized and evaluated. Such thalidomide analog compounds show enhanced potency in the inhibition of angiogenesis without the undesirable effects of administration of thalidomide.

Detection and Quantification of Cripto-1 in Human Milk Using ELISA

Caterina Bianco, David S. Salomon (NCI)
DHHS Reference No. E–290–00/0 filed 26 Jan 2001
Licensing Contact: Matthew Kiser; 301/496–7735 ext. 224; e-mail: kiserm@od.nih.gov

Cripto-1 (CR1) is a member of the epidermal growth factor (EGF)-related families of peptides and is involved in the development and progression of various human carcinomas. In particular, CR1 overexpression has been detected in 50–90% of carcinomas of the colon, pancreas, stomach, gallbladder, breast, lung, endometrium and cervix. Current methodologies of cancer detection, e.g. immunohistochemistry, can be time consuming, inconvenient and oftentimes, inaccurate, and therefore, a need exists for more efficient, reliable and less time consuming methods of detection. The invention relates to such a method of detection. The inventors