of detecting nucleic acid and amino acid sequences as well as modulators of such PTC taste receptors. The ability to taste PTC has been shown to be correlated with the ability to taste other bitter substances, many of which are toxic. Thus variation in PTC perception and knowledge of the genetic basis of these variants can be used to aid the development of a variety of taste improvements in foods and orally administered medications.


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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

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. 202 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.

ADDRESS: 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.

Thalidomide Analogs


Inflammatory processes associated with the over-production of cytokines, particularly of tumor necrosis factor-alpha (TNF-a), accompany numerous neurodegenerative diseases, such as Alzheimer’s disease and ALS, in addition to numerous common systemic conditions, such as rheumatoid arthritis, septic shock, graft-versus-host disease, Crohn’s disease and erythema nodosum leprosum (ENL). TNF-a has been validated as a drug target with the development of the inhibitors Enbrel (Amgen, Thousand Oaks, CA/Wyeth, Princeton, NJ) and Remicade (Centocor, Malvern, PA/Schering-Plough, Orange, NJ) as prescription medications for rheumatoid arthritis. Both, however, are large macromolecules and hence are expensive to produce, require direct intravenous or subcutaneous injection, and have negligible brain access. The classical orally active drug, thalidomide (N-a-phthalimidoglutaramide), a glutamic acid derivative, is being increasingly used in the clinical management of a wide spectrum of immunologically-mediated and infectious diseases, and cancers. Its clinical value in treating ENL derives from its TNF-a inhibitory activity. Specifically, it inhibits TNF-a protein expression at the post-transcriptional level by facilitating turnover of the mRNA (Sampaio et al., 1991 & 1993; Moreira et al., 1993). More recent research has shown similar inhibitory action of COX2 protein expression (Fujita et al., 2001). These actions are mediated post-transcriptionally via AU-rich elements found in the 3′ untranslated regions (3′–UTRs) of each mRNA (Kruys et al., 1994; Chen et al., 1995). Thalidomide’s anti-angiogenesis activity derives from its inhibitory actions on basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) (D’Amato et al., 1994; Figg et al., 2002). The agent, additionally, acts as an inhibitor of the transcription factor, NFκB and a co-stimulator of both CD8+ and CD4+ T cells (Haslett et al., 1998). However, the action of thalidomide to lower TNF-a levels and inhibit angiogenesis is not particularly potent and it therefore represents an interesting lead compound for medicinal chemistry.

Novel structural modification of thalidomide was achieved through the discovery of original and potent isosteric analogues. The present invention relates to thalidomide analogues and, in particular, thiothalidomides (sulfur-containing thalidomide analogues), methods of synthesizing the analogues, and methods for using the analogues to modulate TNF-α and angiogenesis activities in a subject. Dislosed analogues potently inhibited TNF-α secretion, compared to thalidomide, via post-transcriptional mechanisms that decreased TNF-α mRNA stability via its 3′–UTR (Zhu et al., 2003). Actions to inhibit angiogenesis were determined in widely accepted ex vivo assays.

Methods and Compositions for Treating Diseases and Disorders Associated With Natural Killer T-Cells

John R. Ortaldo, Robert H. Wiltrout (NCI)


The invention relates to the discovery that C12 beta-D-galactosyl ceramide may be used to deplete or inactivate NKT cell populations. These findings suggest methods for using C12 beta-D-galactosyl ceramide to treat conditions that would benefit from depletion of NKT cells, such as certain auto-immune diseases (e.g. lupus, MS) and AIDs. The presence of NKT cells can be associated with either beneficial effects or pathology. Deficiencies in NKT cells are associated with at least some types of autoimmune disease, including type 1 diabetes and autoimmune gastritis in mice. In contrast, NKT cells augment autoantibody secretion and lupus development in lupus-prone mouse models and therefore lupus patients may benefit from the depletion of NKT cells. The remission state of multiple sclerosis (MS) is also associated with decreased levels of NKT cells, suggesting NKT cell depletion as a method of treatment for MS.

The above-mentioned invention is available for licensing on an exclusive or a non-exclusive basis.

Leu574 of HIF-1alpha as a Molecular Basis for Therapeutic Application

L. E. Huang (NCI)


The hypoxia-inducible factor 1 (HIF–1) is a transcription factor that plays a pivotal role in cellular adaptation to oxygen availability. HIF–1alpha protein is a subunit of HIF–1. Although the gene for HIF–1alpha is constitutively expressed, it is an extremely short-lived protein under normoxic conditions and is targeted for destruction via the proteasome pathway by an E3 ubiquitin ligase (the VHL protein).

The invention relates to the discovery that mutations or deletions of Leu574 result in a more stable form of HIF–1alpha. Therefore, the invention relates
to methods and compositions for modulating oxygen homeostasis for therapeutic application. In one aspect, the inventors contemplate the use of a more stable form of HIF-1alpha protein for therapeutic angiogenesis purposes such as may be useful in ischemic vascular disease. In another aspect, the inventors contemplate the use of this particular site in a screen for targeted drugs that modulates HIF-1alpha activity. The inventors also suggest that Leu574 could be used for developing drugs targeted to HIF hydroxylase binding, thereby altering HIF-1alpha stability.

This technology is available for licensing on an exclusive or a non-exclusive basis.

**Vasostatin as Marrow Protectant**

Giovanna Tosato *et al.* (NCI)


Licensing Contact: Matthew Kiser; 301/435–5236; kiserm@mail.nih.gov.

This patent relates to the stimulation of hematopoiesis, more specifically to the protection of hematopoietic stem cells from toxic agents, including chemotherapeutic agents and/or irradiation. The subject patent discloses specific fragments of vasostatin, and their application as stimulants of hematopoiesis in vitro and in vivo. Also disclosed is a method for stimulating the proliferation/survival of hematopoietic cells exposed to a chemotherapeutic agent or irradiation using these fragments. In one embodiment, a method is disclosed for stimulating the growth or survival of hematopoietic stem cells with a fragment of vasostatin, in the presence of a growth factor.


**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.

**ADDITIONAL INFORMATION:**

**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; telephone: 301/496–7057; fax: 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

**A Microfluidic Flow-Through Immunoassay for a Simultaneous Detection of Multiple Proteins in a Sub-Microliter Biological Sample**

Nicole Y. Morgan *et al.* (NIH/NIST)


Licensing Contact: Michael Ambrose; 301/594–6565; ambrose@mail.nih.gov.

This invention presents a high throughput, multi-analyte microfluidic chip device. This device can be used for the detection and characterization of proteins, immuno-affinity assays as well as analyte detection in biological samples or other media. The sub-microliter volumes for use make this device applicable where biological samples are rare and difficult to obtain. The device consists of a series of channels that are connected via communication ports for sample flow. The channels can be individually loaded with detection reagents via portals at their ends. As such, the assay channels can be run in series using a single sample source or individually via the loading ports, thus increasing the utility of the microchip device. Each channel can then be detected via colorimetric, fluorimetric or other detection method as desired. The chip can be integrated into multiple detection devices or other analytical equipment. The chip as designed, is manufactured using photolithographic etching, thus the number and size of the individual reaction channels can be modified to increase the number of channels or the volume the channels can hold. The chip should also be reusable, thus further increasing the utility of the device.

**Method for Analysis of Biomarkers Concentrated With Biomarker Attractants**

Arpita Mehta *et al.* (NCI)


Licensing Contact: Fatima Sayyd; 301/435–4521; sayyd@mail.nih.gov.

Biological fluids are the repositories of vast number of molecules that are excreted or otherwise shed by cells. These molecules present in biological fluids reflect the physiological and pathological states of the cells that are in contact by the fluids or the cells from which these molecules are derived. A major goal of clinical diagnostics is to correlate the particular molecules (biomarkers) present in biological fluids with particular disease states.

The present invention relates to analysis of molecules present in biological fluids. Specifically, it discloses a diagnostic method for isolating/analyzing biomarker attractant molecules for the presence of bound fragments of cellular proteins that are known to correlate with particular biological states in specific anatomic or physiologic locations.

**Regulation of RNA Stability**

Wi Lai *et al.* (NIEHS)


Licensing Contact: Jesse S. Kindra; 301/435–5559; kindraj@mail.nih.gov.

This invention relates to the discovery that tristetraprolin (TTP) can promote the poly(A)RNase (PARN) mediated deadenylation of polyadenylated substrates containing AU-rich elements (AREs). As one aspect of the invention, the inventors have developed a cell free system that may be used for the purposes of assessing the effects of the various system components or their derivatives (i.e. AREs, PARN, or TTP) on the deadenylation process or the effects of various test agents on the deadenylation process. Aspects of this work have been published as follows: Lai et al., 2003, Tristetraprolin and Its Family Members Can Promote the Cell-Free Deadenylation of AU-Rich Element-Containing mRNAs by Poly(A) Ribonuclease, MCB 23(11):3798–3812.

This technology is available for licensing on an exclusive or a non-exclusive basis.