The action of Tumor Necrosis Factor alpha (TNF-α) has been implicated in such diseases as arthritis, sepsis, ulcerative colitis, multiple sclerosis, Crohn's disease, septic shock, graft rejection, cachexia, insulin resistance, post-ischemic reperfusion injury, tumor metastasis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurismal aortic disease, degenerative cartilage loss, demyelinating diseases of the nervous system, and HIV infection. TNF-α converting enzyme (TACE) or ADAM 17 (A Disintegrin And Metalloprotease) is a member of a family of zinc metalloproteases, and is an important regulator of inflammation, immune regulation, and cellular proliferation as a consequence of its ability to catalyze the activation of TNF-α from a membrane bound to a soluble form.

The NIH announces the identification of a protein, corresponding to the amino-terminus of the TACE prodomain, that possesses a TACE inhibitory activity that is independent of a cysteine-switch mechanism. This TACE inhibitory protein could be used as a new therapeutic agent against chronic inflammatory diseases that are mediated by TNF-α.

Use of Smad3 Inhibitor in the Treatment of Fibrosis Dependent on Epithelial to Mesenchymal Transition as in the Eye and Kidney

Anita Roberts (NCI).
U.S. Provisional Patent Application No. 60/441,297 filed 17 Jan 2003 (DHHS Reference No. E–062–2003/0–US–01).
Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@od.nih.gov.*

Fibroid scar tissue has been associated with wound healing of the epithelial layer following tissue damage created by surgery or other means. Examples of which include the opaque scar tissue associated with cataract surgery and the fibroid scar tissue produced in several kidney diseases such as is seen in unilateral ureteral obstruction.

Smad2 and Smad3 are highly homologous cytoplasmic proteins which function to mediate signals from Transforming Growth Factor Beta (TGF-β) and activin receptors to promoters of target genes found in the nucleus. The NIH announces a technology wherein Smad 3 is now implicated in TGF-β-dependent transdifferentiation of epithelial cells to mesenchymal cells (EMT), which blocks the endpoint of fibrosis at an early stage of differentiation of epithelial cell precursors into interstitial fibroblasts. In particular, fibrosis was blocked following wounding of the lens of the eye and damage created to the kidney. It is believed that an inhibitor of Smad 3 could be used to block fibrosis following cataract surgery and lens implantation in patients, as well as slowing the progression of end-stage renal disease.

Dated: October 28, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–28055 Filed 11–6–03; 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 invention listed below is owned by an agency of the U.S. Government and is 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 application 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 application.

Cytotoxic Indeno- and Isoindenoisoquinoline Compounds

Yves G. Pommier (NCI).
U.S. Provisional Patent Application No. 60/469,718 filed 12 May 2003 (DHHS Reference No. E–253–2003/0–US–01).
Licensing Contact: George Pipia; 301/435–5560; *pipiag@mail.nih.gov.*

The present invention is directed to novel indeno- and isoindenoisoquinoline compounds, their derivatives and their pharmaceutical formulations having anticancer activity, as well as methods of treating cancer. The invention is also directed to methods of preparing these novel compounds. These compounds have been tested against 55 tumor cell lines and have been found to have a strong activity against a wide variety of tumor cell lines, including lung, colon, central nervous system, melanoma, ovarian, renal, prostate and breast cancers, compared with 2-methoxy estradiols. Some of these compounds target topoisomerase I and remain active in camptothecin-resistant cancer cells. It is expected that these compounds will be very useful in the treatment of a wide variety of cancers.

Identification of Novel Birt-Hogg-Dubé (BHD) Gene

Laura S. Schmidt (NCI).
PCT Application No. PCT/US03/17227 filed 30 May 2003 (DHHS Reference No. E–190–2002/2–PCT–01).
Licensing Contact: George Pipia; 301/435–5560; *pipiag@mail.nih.gov.*

Birt-Hogg-Dubé (BHD) syndrome is an inherited autosomal dominant neoplasia syndrome characterized by benign hair follicle tumors and is associated with a higher risk for developing renal cancer, spontaneous pneumothorax and/or lung cysts.

The present invention describes identification of the BHD syndrome associated germline mutations in a novel human gene, herein called BHD gene. This gene encodes for the protein, folliculin, functions of which remain currently unknown.

This discovery makes possible the development of a diagnostic method for BHD syndrome using a simple blood test. The test is particularly useful in detecting BHD mutations in asymptomatic carriers within BHD families.

Patients with kidney tumors can be evaluated for BHD gene mutations using a similar genetic diagnostic test, which will allow for a more accurate diagnosis of a kidney cancer and improved patient prognosis. The BHD encoding sequence is the third gene found to be responsible for inherited kidney cancer, and mutation testing allows for a correct diagnosis and initiation of the proper treatment, which is different for each of the types of kidney cancer caused by the three genes.

Methods of using BHD encoding sequence also allows for a differential genetic diagnosis of spontaneous pneumothorax, or collapsed lung. Since collapsed lung can be caused by several factors, a BHD diagnostic test allows a physician to determine predisposition to and possible recurrence of additional spontaneous pneumothoraces due to mutation(s) in the BHD gene.

The discovery should also lead to the development of novel pharmaceutical products and methods for treating BHD skin lesions using creams containing the BHD gene product, folliculin. Such products and methods of treatment are expected to reduce the size and appearance of the benign hair follicle tumors.

The disclosed technology will provide new and exciting methodologies to correctly diagnose BHD syndrome and should lead to the development of novel pharmaceutical reagents for treatment of BHD skin lesions as well as other skin diseases.

This research is also described in: Nickerson *et al., Cancer Cell* 2: 157, 2002; Zbar *et al., Cancer Epidem. Bio. Prev.* 11: 393, 2002; Schmidt *et al., Am. J. Hum. Genet.* 69: 876, 2001; Toro *et al., Arch. Dermatol.* 135: 1195, 1999.

Dated: October 27, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–28056 Filed 11–6–03; 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 invention listed below is owned by an agency of the U.S. Government and is 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 application 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 application.

B-Defensins as Activators of Dendritic Cells and Vaccine Carrier

Arya Biragyn and Larry Kwak (NCI).

U.S. Provisional Application No. 60/421,488 filed 25 Oct 2002 (DHHS Reference No. E–342–2002/0–US–01).

Licensing Contact: Catherine Joyce; 301/435–5031; e-mail: *joycec@mail.nih.gov.*

Tumor antigens are known to be poorly immunogenic and attempts to elicit immune responses against the epitopes of antigens specific to tumor cells have been largely unsuccessful. The inventors have developed a cancer vaccine comprising a defensin fused to a tumor antigen or viral antigen to enhance the immunogenicity of the tumor antigen or viral antigen. The inventors have demonstrated, with animal data, that chimeric proteins comprising a defensin fused to a model tumor antigen (lymphoma-derived single-chain Fv) generate a measurable humoral and anti-tumor cellular immune response when administered to a subject. (Biragyn *et al.,* Mediators of innate immunity that target immature, but not mature, dendritic cells induce antitumor immunity when genetically fused with nonimmunogenic tumor antigens, *J. Immunology* 2001 Dec 1, 167(11):6644–6653. Also, Biragyn *et al.,* DNA vaccines encoding human immunodeficiency virus-1 glycoprotein 120 fusions with proinflammatory chemoattractants induce systemic and mucosal immune responses, *Blood* 2002 Aug 15 100(4):1153–1159.)

Recently the inventors have further discovered that murine beta-defensin 2 acts directly on immature dendritic cells as an endogenous ligand for Toll-like receptor 4 (TLR–4), inducing up-regulation of costimulatory molecules and dendritic cell maturation. (Biragyn *et al.,* Toll-like receptor 4-dependent activation of dendritic cells by beta-defensin 2, *Science* 2002 Nov 1, 298(5595):1025–1029).

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

Dated: October 24, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–28057 Filed 11–6–03; 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.

Putative PEDF Receptor

Sofia P. Becerra, Luigi Notari (NEI).

DHHS Reference No. E–314–2003/0–US–01 filed 07 Aug 2003.

Licensing Contact: Susan S. Rucker; 301/435–4478; *ruckersu@mail.nih.gov.*

This application describes compositions and methods related to Pigmented Epithelium Derived Factor (PEDF). PEDF is a protein, belonging to the serpin family, that has been demonstrated to have neurotrophic, gliastatic, neuronotrophic and anti-angiogenic properties. In particular, the compositions and methods described and claimed in this application are related to the isolation, cloning, expression and characterization of the putative receptor for PEDF. The PEDF receptor as described herein is a transmembrane protein having an extracellular ligand-binding domain, a transmembrane domain and an intracellular domain. The PEDF receptor shares some homology with an orphan receptor identified in the liver and the protein known as adiponutrin.

The isolation and cloning of the PEDF receptor will be useful in basic research to further elucidate the role of PEDF and its receptor in signal transduction