cell migration, maturation, and a production of a wide variety of cytokines. Based on these potent chemotactic and activating effects on dendritic cells, EDN might be useful as a clinical immunoadjuvant for the promotion of immune responses to specific antigens of tumors or pathogenic organisms.

Protein Kinase C Inhibitor, Related Composition, and Method of Use

Shaomeng Wang, Peter Blumberg (NCI), Nancy Lewin (NCI).
U.S. Provisional Patent Application No. 60/451,214 filed 28 Feb 2003 (DHHS Reference No. E–073–2003/0–US–01).
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

Protein kinase C is a critical component in cellular signaling, involved in cellular growth, differentiation, and apoptosis. It has been identified as a promising therapeutic target for cancer, diabetic retinopathy, and Alzheimer's disease, among other indications.

This invention relates to lead compounds that can inhibit protein kinase C isoforms through disruption of their C1 domains. The inventors also found that these compounds possess isoform selectivity, an important feature for therapeutic specificity. Finally, although the disclosed compounds are previously known molecules, novel structures are described in the invention that have further improved specificity.

Applications for the HMGN1 Pathway

Michael Bustin (NCI).
U.S. Provisional Patent Application No. 60/455,728 filed 17 Mar 2003 (DHHS Reference No. E–208–2002/0–US–01).
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

HMGN1 is a protein that binds to nucleosomes, changes chromatin structure and affects transcription, and the expression of this protein changes during differentiation. Mice lacking this protein have increased growth capacity of several skin components, including epidermis, epidermal appendages, and dermis. Conceivably, this change could be related to an alteration of stem cell differentiation or to cell cycling events. The current invention relates to interference with this pathway, which might lead to increased stem cell differentiation and increased hair cycling and growth in humans as well. This invention might be useful to increase hair growth, enhance wound healing for epidermal and dermal wounds, and enhance stem cell populations for tissue regeneration, gene targeting, or gene therapeutic indications.

Novel Stable Anti-CD22 Antibodies

Susanna Rybak, Juergen Krauss, Michaela Arndt (NCI).
U.S. Provisional Application No. 60/387,306 filed 06 Jun 2002 (DHHS Reference No. E–055–2002/0–US–01); PCT Patent Application PCT/US03/18201 filed 06 Jun 2003 (DHHS Reference No. E–055–2002/0–PCT–02).
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

The current invention relates to engineered LL2 single chain antibodies possessing improved and/or unexpected properties. The first embodiment includes engineered single chain antibodies that have enhanced stability. Specific VH and VL residues were identified which might contribute to the instability, and these were substituted to create scFv variants with improved stability and biological half-life. In the second embodiment, an LL2 single chain Fv antibody was engineered with no linker between the VH and VL sequences. The antibody exhibited the surprising property of acting as a monomer (rather than a trimer or tetramer) and retained specific binding to CD22. This invention might be useful as a general method to produce therapeutic antibodies or immunoconjugates more easily, and for such antibodies or immunoconjugates to be more stable *in vivo.*

Dated: October 30, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–28054 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.

Isolation of Hybridomas Producing Monoclonal Antibodies (MAbs) Inhibitory to Human CYP2J2

Dr. Darryl Zeldin (NIEHS), Dr. Harry Gelboin (NCI), *et al.*
DHHS Reference No. E–337–2003/0—Research Tool.
Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@mail.nih.gov.*

Cytochromes P450 catalyze the NADPH-dependent oxidation of arachidonic acid to various eicosanoids found in several species. The eicosanoids are biosynthesized in numerous tissues including pancreas, intestine, kidney, heart, and lung where they are involved in many different biological activities.

The NIH announces three specific monoclonal antibodies that strongly inhibit and/or immunoblot the human cytochrome P450 2J2 (CYP2J2). MAb 6–5–20–8 selectively inhibits CYP2J2-mediated arachidonic acid metabolism by more than 80% and also immunoblots the enzyme. MAb 6–2–16–1 also selectively inhibits arachidonic acid metabolism by more than 80%, but does not immunoblot the enzyme. MAb 5–3–2–2 is not inhibitory, but selectively immunoblots the enzyme. These antibodies can be used to identify and quantify inter-individual variation in physiological functions and to study pharmacological drug metabolism in various tissues.

This research is also described in: Sun *et al.*, *Circ. Res.* 90: 1020–1027, 2002; King *et al.*, *Mol. Pharmacol.* 61: 840–852, 2002; Yang *et al.*, *Mol. Pharmacol.* 60: 310–320, 2001; Zeldin, *J. Biol. Chem.* 276: 36059–36062, 2001; Node *et al.*, *J. Biol. Chem.* 276: 15983–15989, 2001; Node *et al.*, *Science* 285: 1276–1279, 1999; Wu *et al.*, *J. Biol. Chem.* 271: 3460–3468.

TNF-α Converting Enzyme Inhibitory Agents and Stimulatory Agents

Dr. Stewart Levine *et al.* (NHLBI).
U.S. Provisional Patent Application filed 24 Sep 2003 (DHHS Reference No. E–208–2003/0–US–01).
Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@mail.nih.gov.*

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.