form; however, when the same peptides are immobilized on a substratum, they promote adhesion and proliferation of endothelial cells. Thus by controlling the conditions, these peptides can be used to generate specific responses. Specific applications for the peptides include the treatment of angiogenesis-mediated diseases, production of vascular grafts and artificial blood vessels.

Redox-Stable, Non-Phosphorylated Cyclic Peptide Inhibitors of SH2 Domain Binding to Target Protein, Conjugates Thereof, Compositions and Methods of Synthesis and Use Serial No. 60/137,187 filed 02 Jun 1999

Peter Roller, Ya-Qiu Long, Feng-Di Lung, Charles R. King (NCI)

The present invention is predicated on the surprising and unexpected discovery of non-phoshorylated cyclic peptide inhibitors of binding SH2 domains in proteins comprising SH2 domains to target proteins which not only are redox-stable *in vivo* but have unprecedented specific binding affinities.

Src homology–2 (SH2) domains selectively bind to phosphotyrosyl (pTyr)-containing regions of target proteins. SH2 binding can modulate: c-src activity; substrate specificity for c-abl proto-oncoproteins; and the transduction of signals initiated by growth factor receptors and cellular attach systems. The SH2 domain of growth factor receptor-bound protein (Grb2) is a specific example which contains one SH2 domain and two src homology–3 (SH3) domains. The prevention of Grb2-mediated multi-protein assemblies is considered a promising therapeutic target for the development of antiproliferative agents directed to cells that over-express growth factor receptors. Previously identified SH2-inhibitors have detectable activity, but their binding affinities are substantially lower than natural ligands. A need therefore exists for more efficient and stable inhibitors, and the technology herein disclosed provides for such inhibitors. Additionally, the technology offers the possibility of conjugates comprising a compound (SH2 inhibitor) and a carrier agent, i.e., signal peptides, antennapedia peptides, or lipofectin. Suitable targets would preferably include, but not necessarily be limited to: growth factor receptors, such as EGFR; morphology determining proxies, such as FAK; a cellular attachment protein; a proto-oncoprotein; an oncoprotein, such as BCR-abl; or a mitogen-activated protein (MAP). In one application of this method, inhibition of the binding of a target protein by an SH2 domain in a protein comprising an SH2 domain prevents cancer, in particular, breast cancer. Administration of the SH2-inhibitor/SH2-conjugate can be accompanied by an anti-cancer agent such as a chemotherapeutic agent, a cytotoxic agent or its prodrug, radiation and/or a radioactive isotope.

Phenylalanine Derivatives

T. Burke *et al.* (NCI)
Serial No. 60/126,047 filed 23 Mar 1999

The present invention relates to novel phenylalanine derivatives, compositions and methods of using said derivatives to inhibit SH2 domain binding with a phosphoprotein. Additionally, the invention provides precursors suitable for preparing these phenylalanine derivatives.

The therapy and prophylaxis of proliferative diseases such as cancer, autoimmune disorders and hyperproliferative skin disorders can involve signal transduction. These signal-pathways are critical to normal cellular homeostasis and are necessary processes for relaying extracellular messages from various sources, e.g., growth factors, hormones or neurotransmitters, via receptors to the interior of the cell. Protein-tyrosine kinases are integral participants of many of these pathways, and they are responsible for the phosphorylation of specific tyrosine residues to form tyrosine phosphorylated residues. These pathways can involve complex networks which contain proteins with specific amino acid sequences called ''Src-homology 2'' (SH2) domains. Malfunctions in these protein-tyrosine phosphorylations through tyrosine kinase overexpression or deregulation, can manifest a variety of oncogenic and proliferative disorders. SH2 domain containing proteins that play roles in cellular signaling and transformation include, but are not limited to: Src, Lck, Ras GTPase-activating protein, Phospholipase C, PI–3 kinase, Grb2, BCR Abl and Tyk2. Central to the binding of SH2 domains with phosphotyrosine (pTyr)-containing ligands is the interaction of a doubly ionized pTyr phosphate with two highly conserved arginine residues. These interactions are critical, and binding is usually lost by removal of the phosphate group. While the pTyr-pharmacophore therefore plays a dominant role in SH2 domain-ligand interactions, pTyr residues are not suitable components of inhibitors intended for *in vivo* application, due to the enzymatic lability of the phosphate ester bond and the poor cellular penetration of the doubly ionized phosphate species. Therefore, a need exists for non phosphate containing compounds that can mimic the structural interactions of phosphotyrosyl residues within SH2 domain pTyr-binding sites, and in so doing disrupt the interactions between SH2 domains of proteins, e.g., Grb2, and proteins with phosphorylated moieties. The disclosed invention provides viable candidates for these compounds and could provide for the development of therapeutic agents for the treatment of proliferative diseases or conditions as well as relevant diagnostic or testing procedures.

Dated: August 17, 1999.

Jack Spiegel,

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

[FR Doc. 99–21889 Filed 8–23–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Meeting

Pursuant to section 10(a) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the President's Cancer Panel.

The meeting will be open to the public, with attendance limited to space available. Individuals who plan to attend and meet special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

Name of Committee: President's Cancer Panel.

Date: September 22, 1999.

Time: 9:00 AM to 4:00 PM.

Agenda: The Changing Face of Public Health—Implications For The National Cancer Program Now And In The Future.

Place: National Institutes of Health, Building 31, C Wing, Conference Room 10, 9000 Rockville Pike, Bethesda, MD 20892.

Contact Person: Maureen O. Wilson, PhD, Executive Secretary, National Cancer Institute, National Institutes of Health, 31 Center Drive, Building 31, Room 4A48, Bethesda, MD 20892.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399,

Cancer Control, National Institutes of Health, HHS)

Dated: August 17, 1999.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 99–21885 Filed 8–23–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Institute Special Emphasis Panel, Evaluation of Chemopreventive Agents by In Vitro Techniques.

Date: September 13, 1999.

Time: 1:00 PM to 2:00 PM.

Agenda: To review and evaluate contract proposals.

Place: 6130 Executive Boulevard, EPN/F, Rockville, MD 20852, (Telephone Conference Call).

Contract Person: Wilna A. Woods, PHD, Deputy Chief, Special Review, Referral and Research Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, Rockville, MD 20852, (301) 496–7903.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: August 17, 1999.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 99–21886 Filed 8–23–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Deafness and Other Communication Disorders; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Communication Disorders Review Committee.

Date: October 13–15, 1999.

Time: 8:00 AM to 5:00 PM.

Agenda: To review and evaluate contract proposals.

Place: River Inn, 924 25th Street, NW, Washington, DC 20037.

Contact Person: Melissa Stick, PHD, MPH, Scientific Review Administrator, NIH/NIDCD/DEA/SRB, 6120 Executive Blvd (EPS/400), Bethesda, MD 20892.

(Catalogue of Federal Domestic Assistance Program Nos. 93.173, Biological Research Related to Deafness and Communicative Disorders, National Institutes of Health, HHS)

Dated: August 17, 1999.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 99–21881 Filed 8–23–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Alcohol Abuse and Alcoholism; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the National Advisory Council on Alcohol Abuse and Alcoholism.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and/or contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications and/or contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Advisory Council on Alcohol Abuse and Alcoholism.

Date: September 15–16, 1999.

Closed: September 16, 1999, 7:00 PM to 9:00 PM.

Agenda: To review and evaluate grant applications.

Place: Bethesda Hyatt Regency, One Bethesda Metro, Bethesda, MD 20814.

Closed: September 16, 1999, 8:30 AM to 9:00 AM.

Agenda: To review and evaluate grant applications and/or proposals.

Place: Natcher Building, Conference Room E1/E2, 45 Center Drive, Bethesda, MD 20892.

Open: September 16, 1999, 9:00 AM to 3:30 PM.

Agenda: Program Developments and Priorities.

Place: Natcher Building, Conference Room E1/E2, 45 Center Drive, Bethesda, MD 20892.

Contact Person: James F. Vaughan, Executive Secretary, National Institute on Alcohol Abuse and Alcoholism; National Institutes of Health, PHS, DHHS; Bethesda, MD 20892.

(Catalogue of Federal Domestic Assistance Program Nos. 93.271, Alcohol Research Career Development Awards for Scientists and Clinicians; 93.272, Alcohol National Research Service Awards for Research Training; 93.273, Alcohol Research Programs; 93.891, Alcohol Research Center Grants, National Institutes of Health, HHS)

Dated: August 17, 1999.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy, NIH.

[FR Doc. 99–21882 Filed 8–23–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Mental Health; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the