stability. Appropriate framework sequences with high sequence identities to the murine antibody to be humanized were then chosen from the pre-selected pool of stable scaffolds. As a result, humanized scFv fragments with low immunogenic potential and high biophysical stability were generated.

In contrast to other methodologies, unusual human framework residues were identified by aligning the human variable domain sequences to several sequence reference templates from antibody repertoires. The structural role of each identified unusual residue was further examined on the basis of information of antibodies with known crystal structures. Several residues were considered critical for interfering with the structural integrity of the antigen binding site and were successively back-mutated to the murine donor sequence. As a result, a panel of three humanized scFv antibodies with nanomolar affinity constants were generated. Importantly, the introduced back-mutations did not alter the biophysical properties of the constructs.

Tumor Suppressor Gene Polypeptides and Related Nucleic Acids, Host Cells, Compositions, and Methods of Use in Inhibition of Cell Growth, Modulation of Gene Expression, and Enhancement of Immune-Response Inducing Effect of a Vaccine

Denise Simmons (NCI)
DHHS Reference No. E–052–02/0 filed 03 May 2002
Licensing Contact: Matthew Kiser; 301/435–5236; *kiserm@od.nih.gov.*

Many cell lines have specific suppressor proteins that can inhibit the proliferation of cancer cells. These regulatory proteins are crucial in maintaining the fine line between appropriate proliferation and over proliferation. It is when these regulatory suppressor proteins become inactivated or over/under expressed that uncontrolled cell growth leading to neoplasia can result.

It has been established that certain suppressor proteins can inhibit cell proliferation: tazarotene-induced gene 3 (H-TIG–3), and Hras Revertant gene 107 (H-rev107). Modification or over/under expression of these proteins can cause excessive cellular proliferation. It is now known that these proteins, as well as a candidate tumor suppressor protein, lecithin:retinol acyl transferase (LRAT) share a homologous region. The subject invention pertains to a group of short polypeptide sequences that are based on this homologous region. These short polypeptides are effective tumor suppressors.

The scope of this invention includes amino acid sequences and the corresponding nucleic acid sequences that encode the polypeptides. Modifications of the polypeptide sequences include both substitution and additions. The subject invention also applies to the method of inhibiting cell growth, a method of modulating gene expression, and a method of enhancing the immune response-inducing effect of a vaccine.

Material and Methods for Inhibiting Wip1

Dimtry V. Bulavin (NCI), Ettore Appella (NCI), Albert Fornace (NCI), Anne Kallioniemi (NCI)
DHHS Reference No. E–002–02/0 filed 22 Mar 2002
Licensing Contact: Matthew Kiser; 301/435–5236; *kiserm@od.nih.gov.*

p53 protein is an attractive cancer-therapeutics target since it is expressed in all normal cells and is important for cancer cell apoptosis (death). The p53 protein provides a cellular self-destruct signal when DNA damage has occurred. Under expression of this protein can cause damaged cells to proliferate causing cancer. A potential proto-oncogene, wild-type p53-induced phosphatase 1 (Wip1), has been implicated in the down regulation of p53. Therapeutic strategies that can block Wip1 will increase the activity of p53 thus preventing cancer cell proliferation in p53 wt tumors that over-express Wip1. The subject invention pertains to isolated and purified oligonucleotides or isolated and purified morpholino oligonucleotides with the ability to inhibit Wip1 expression. These oligomers can be used for the treatment of cancer. In addition to practical uses of the oligomers, a methodology for screening standard and morpholino oligonucleotides for Wip1 inhibition is included. Finally, a methodology to test the efficacy of standard and morpholino test oligonucleotides completes this invention.

Attenuated and Dominant Negative Variant cDNAs of STAT6: STAT6b and STAT6c

William LaRochelle, Bharvin K.R. Patel, Jacalyn H. Pierce (all of NCI)
Serial No. 09/511,625 filed 23 Feb. 2000, now U.S. Patent 6,368,828 issued 09 Apr. 2002.
Licensing Contact: Susan S. Rucker; 301/435–4478; *ruckers@od.nih.gov.*

This patent relates to signal transduction pathways. In particular, the patent relates to transcription factors. The transcription factors described in the patent are members of the family of transcription factors known as Signal Transducers and Activators of Transcription (STATs). More particularly, the patent discloses the identification, isolation, sequencing and cloning of cDNAs that encode naturally occurring variants, Stat6b and Stat6c, of the protein STAT6.

The Stat6b variant contains an NH_2 terminal deletion of naturally occurring Stat6. The Stat6c variant contains an internal deletion, within the SH2 domain, of naturally occurring Stat6. The naturally occurring variants exhibit different properties. Stat6b acts as an attenuated variant, with respect to IL–4 induced MHC class II and Fc receptor cell surface expression, promoter binding and transcriptional activation when compared to Stat6. Stat6c acts as a dominant negative variant with respect to IL–4 mediated up-regulation of the cell surface antigens CD16/CD32 and CD23. The role of both variants in mediating IL–4 activity suggests that either could be useful in developing drugs for targeting diseases involving inflammatory and cell-mediated immune responses such as asthma.

The patent includes claims to the Stat6 variant polypeptides, the nucleic acids, vectors for expression of the variants, cells into which the variants have been introduced and methods of producing the Stat6 variant polypeptides.

This work has been published in part at B.K.R. Patel *et al.*, PNAS USA 95: 175–77 (Jan. 1998).

Dated: March 12, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–6443 Filed 3–17–03; 8:45 am]

BILLING CODE 4140–01–P

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, Novel Technologies for Noninvasive Detection, Diagnosis and Treatment of Cancer.

Date: April 21, 2003.

Time: 8 a.m. to 7 p.m.

Agenda: To review and evaluate contract proposals.

Place: National Cancer Institute, 6130 Executive Plaza North, Executive Blvd., Conference Room H, Rockville, MD 20852.

Contact Person: Sherwood Githens, PhD, Scientific Review Administrator, Special Review and Logistics Branch, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard, Room 8068, Bethesda, MD 20892, (301) 435–1822.

(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: March 12, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03–6435 Filed 3–17–03; 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 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: National Cancer Institute Initial Review Group, Subcommittee A—Cancer Centers.

Date: April 14–15, 2003.

Time: 7:30 a.m. to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: Double Tree Rockville, 1750 Rockville Pike, Rockville, MD 20852.

Contact Person: David E. Maslow, PhD, Scientific Review Administrator, Grants Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard—Room 8117, Bethesda, MD 20892–7405, (301) 496–2330.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

(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: March 12, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03–6437 Filed 3–17–03; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Center for Complementary and Alternative Medicine; Notice of Closed Meetings

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 meetings.

The meetings 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: National Center for Complementary and Alternative Medicine Special Emphasis Panel.

Date: March 24, 2003.

Time: 7 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Bethesda Marriott Suites, 6711 Democracy Boulevard, Bethesda, MD 20817.

Contact Person: Carol Pontzer, Scientific Review Administrator, National Center for Complementary and Alternative Medicine, 6707 Democracy Blvd., Bethesda, MD 20892.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Center for Complementary and Alternative Medicine Special Emphasis Panel, AIDS/HIV.

Date: April 2–3, 2003.

Time: 7 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Bethesda Marriott Suites, 6711 Democracy Boulevard, Bethesda, MD 20817.

Contact Person: Dale Birkle, Scientific Review Administrator, NIH/NCCAM, 6707 Democracy Blvd., Democracy Two Building, Suite 401, Bethesda, MD 20892, (301) 451–6570, *birkled@mail.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Dated: March 11, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03–6353 Filed 3–17–03; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Eye 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 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: National Eye Institute Special Emphasis Panel, Small Grants for Pilot Research R03 Applications.

Date: April 3–4, 2003.

Time: April 3, 2003, 8 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn Select Bethesda, 8120 Wisconsin Ave., Bethesda, MD 20814.

Time: April 4, 2003, 8 a.m. to 5 p.m.