the current Oka vaccine strain that it is markedly impaired for establishing latency. This virus may be a safer vaccine than the currently available vaccine.

Recombinant of Respiratory Syncytial Virus (RSV) Expressing Green and/or Red Fluorescent Protein

Mark Peeples (Rush Presbyterian-St. Luke's Medical Center) and Peter Collins (NIAID)
DHHS Reference No. E–038–2002/0 (Research Materials)
Licensing Contact: Susan Ano; 301/435–5515; *anos@od.nih.gov.*

The biological materials RSV expressing green and/or red fluorescent proteins are available for licensing as research tools for antiviral drug screening or for studying infection and replication of the virus in real time in cultured cells. RSV is the most important viral respiratory pathogen in infants and thus is a major target for development of antiviral agents. The fluorescent protein markers allow rapid quantification of the extent of virus infection and are easily used in conjunction with common apparatuses such as 96-well plates and fluorescence plate readers.

These viruses are produced by the reverse genetic system as described in U.S. patent 6,264,957 (issued July 24, 2001) to Dr. Peter Collins of the NIAID. This reverse genetic system is also available for licensing (DHHS Ref. E–187–1995/1), including all of the plasmids necessary to make the recombinant viruses.

This research has been described, in part, in Hallak et al., Virology 271:264–275, 2000; Zhang et al., J. Virol. 76:5654–5666, 2002; Techaarpornkul et al., Virology 294:296–304, 2002.

HIV–1 Reverse Transcriptase Expression Systems

Dr. Stephen Hughes et al. (NCI)
DHHS Reference No. E–034–91/0
Licensing Contact: Sally Hu; 301/435–5606; *hus@od.nih.gov.*

This invention describes a series of HIV–1 reverse transcriptase (RT)-based products:

(a) HIV–1 RT (66 kDa) and HIV–2 RT (68 kDa) expression plasmids. These lead to the production of homodomeric forms of these proteins.

(b) Inducible expression plasmid p66his-prot producing large amounts of HIV–1 RT (p66) and small amounts of HIV–1 protease. This leads to the production of a p66/p51 heterodimeric form of the protein. A version of this plasmid is available with 6x his tail on p66 to simplify purification of the heterodimer. Expression plasmids for wild-type RT and for numerous mutated RT, including most of the common drug resistant mutants, are available. Mutated RT forms: AZT–21; HIV–2 (His); L74V; P236L; L100I; K103N; V106A; E138K; V181I; M184V; Y188L.

(c) HIV–1 RT with a substitution C280S and a double mutant C38V/C280S that are less susceptible to oxidation than the wild-type enzyme. These mutant HIV–1 RTs have enzymatic properties that are similar to wild-type HIV–1 RT.

Those RT expression plasmids might be used both in biological and medical research such as to study various properties of the enzyme, to determine which domains of the enzyme are the most promising for directing anti-RT reagents against, and to screen RT inhibitors *in vitro.* The HIV–1 Reverse Transcriptase Expression plasmids subject of this report are available for licensing via biological material licenses (BML).

Dated: March 11, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–6442 Filed 3–17–03; 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.

IL–21 Critically Regulates Immunoglobulin Production

Warren J. Leonard, Katsutoshi Ozaki, and Rosanne Spolski (NHLBI)
U.S. Provisional Patent Application 60/393,215 filed 01 Jul 2002
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@od.nih.gov.*

The invention includes a mouse in which the IL–21 receptor gene is disrupted by homologous recombination, the disruption being sufficient to prevent expression of the IL–21 receptor and thus to inhibit the action of IL–21. The invention also includes a mouse in which both the IL–21 receptor gene and the IL–4 gene are simultaneously disrupted in fashions being sufficient to inhibit the action of IL–21 and the production of IL–4. In a homozygous state, these mutations produce a mouse that has diminished B cell function.

This invention also relates to the use of agents that inhibit the interaction of IL–21 with the IL–21 receptor to modulate an immune response. This invention may be used to alter B cell activity, to treat a subject with Job's disorder, to treat an allergic reaction in a subject, or prevent an allergic reaction in a subject.

Grafting of a Murine Antibody Onto a Human Framework

S. Rybak, J. Krauss, M. Arndt, and A. Martin (NCI)
U.S. Provisional Patent Application 60/390,033 filed 17 June 2002
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@od.nih.gov.*

This invention relates to humanization of antibodies specifically providing novel biophysically stable human framework sequences that can be used to humanize antibody single chain Fv (scFv) fragments. An exemplary RFB4 humanized scFv antibody was constructed using the new sequences. The novel sequences were obtained after stringent panning of a human phage display library on (irrelevant) antigen. These antibody variable domain frameworks were subsequently used as human acceptor scaffolds for grafting the murine antibody specificity. The general approach described here differs from other humanization procedures wherein appropriate human acceptor scaffolds are selected from either antibodies with solved crystal structures or (germline) sequence databases. In the current invention, human acceptor frameworks were first pre-selected for

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