

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

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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

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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

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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 NH₂ 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.

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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