Practical Approach, Irl Press; D. M. J. Lilley and J. E. Dahlberg, 1992, *Methods of Enzymology: DNA Structure Part A: Synthesis and Physical Analysis of DNA* Methods in Enzymology, Academic Press; Using Antibodies: A Laboratory Manual: Portable Protocol NO. I by Edward Harlow, David Lane, Ed Harlow (1999, Cold Spring Harbor Laboratory Press, ISBN 0-87969-544-7); Antibodies: A Laboratory Manual by Ed Harlow (Editor), David Lane (Editor) (1988, Cold Spring Harbor Laboratory Press, ISBN 0-87969-314-2), 1855. Handbook of Drug Screening, edited by Ramakrishna Seethala, Prabhavathi B. Fernandes (2001, New York, NY, Marcel Dekker, ISBN 0-8247-0562-9); and Lab Ref: A Handbook of Recipes, Reagents, and Other Reference Tools for Use at the Bench, Edited Jane Roskams and Linda Rodgers, 2002, Cold Spring Harbor Laboratory, ISBN 0-87969-630-3. ~~Each of these general texts is herein incorporated by reference.~~

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a diagram showing that PRL-3 mAb effectively inhibits the formation of metastatic tumors formed by PRL-3 expressing cancer cells. A, Total cell lysates were prepared from B16F0 and B16F10 melanoma cancer cells and endogenous PRL-3 protein expression was determined using immunoblot. GAPDH was used as a loading control. B, C57BL6 mice were injected with $1x10^6$ B16F0 cells (on day 1) followed by PRL-3 mouse antibody (mAb, clone #318) treatment with therapeutic plan. C. On day 17-20, tumors were frequently found in the lung, liver, adrenal gland, kidney, and bone in untreated mice (n=5), while the PRL-3 mAb eliminates the formation of tumors in most tissues of treated mice (n=5). D, The body weight of PRL-3 mAb 'treated' B16F0 recipient mice constantly increased throughout the duration of the experiment. E, Parallel experiments were performed with non-PRL-3 expressing B16F10 melanoma cancer cell line and no therapeutic outcome was obtained with PRL-3 mAb therapy. F, The body weights of both treated and untreated B16F10 receipt mice constantly decreased over the duration of the experiment.

Figure 2 is a diagram showing that B-cells are important in mediating the antibody therapeutic event. A. Kaplan-Meier survival curves were used to compare the 'treated' and 'untreated' groups of B-cell deficient muMT mice injected with B16F0 cells. No difference in

such as Fibrosarcoma, myxosarcoma, liposarcoma, lymphangioendotheliosarcoma, angiosarcoma, endotheliosarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, lymphangiosarcoma, synovioma, mesothelioma, leimyosarcoma, rhabdomyosarcoma, colon carcinoma, ovarian cancer, prostate cancer, pancreatic cancer, breast cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, choriocarcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma seminoma, embryonal carcinoma, cervical cancer, testicular tumour, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, ependymoma, pinealoma, hemangioblastoma, acoustic neuoma, medulloblastoma, craniopharyngioma, oligodendroglioma, menangioma, melanoma, neutroblastoma and retinoblastoma.

The antibody approach to therapy involving use of anti-intracellular oncoprotein antibodies may be combined with other approaches for therapy of such disorders including expression of anti-sense constructs directed against intracellular oncoprotein polynucleotides as described here, and administering them to tumour cells, to inhibit gene function and prevent the tumour cell from growing or progressing.

Anti-sense constructs may be used to inhibit gene function to prevent growth or progression in a proliferative cell. Antisense constructs, *i.e.*, nucleic acid, such as RNA, constructs complementary to the sense nucleic acid or mRNA, are described in detail in US 6,100,090 (Monia *et al.*), and Neckers *et al.*, 1992, *Crit Rev Oncog* 3(1-2):175-231~~, the teachings of which document are specifically incorporated by reference~~.

In a particular example, cancer may be treated or prevented by reducing the amount, expression or activity of intracellular oncoprotein in whole or in part, for example by siRNAs capable of binding to and destroying intracellular oncoprotein mRNA.

RNA interference (RNAi) is a method of post transcriptional gene silencing (PTGS) induced by the direct introduction of double-stranded RNA (dsRNA) and has emerged as a useful tool to knock out expression of specific genes in a variety of organisms. RNAi is described by

~~Each of the applications and patents mentioned in this document, and each document cited or referenced in each of the above applications and patents, including during the prosecution of each of the applications and patents ("application cited documents") and any manufacturer's instructions or catalogues for any products cited or mentioned in each of the applications and patents and in any of the application cited documents, are hereby incorporated herein by reference. Furthermore, all documents cited in this text, and all documents cited or referenced in documents cited in this text, and any manufacturer's instructions or catalogues for any products cited or mentioned in this text, are hereby incorporated herein by reference.~~

Various modifications and variations of the described methods and system of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the claims.

CLAIMS

~~1. Use of an antibody therapy for targeting intracellular oncoproteins or proteins to prevent cancer metastasis.~~

~~2. Use of an vaccine therapy comprising an oncoprotein protein for vaccination to stimulate a host to produce its own antibodies to prevent tumor formation.~~

~~3. Use according to Claim 1, in which the antibody therapy is an intracellular antibody therapy.~~

~~4. Use according to Claim 2, in which the vaccine therapy is an intracellular vaccine therapy.~~

~~5. A method of treatment of cancer, such as metastatic cancer, in an individual suffering or suspected to be suffering from cancer, the method comprising administering a therapeutically effective amount of an antibody capable of binding to an intracellular oncoprotein to the individual.~~

~~6. A method according to Claim 5, in which the antibody is capable of binding to an intracellular oncoprotein, preferably by being capable of crossing the plasma membrane of a cell.~~

~~7. A method according to Claim 5 or 6, in which the antibody comprises a monoclonal antibody, a chimeric antibody or a humanised antibody.~~

~~8. A method according to Claim 5, 6 or 7 in which the antibody is capable of binding to and inhibiting a biological activity of the intracellular oncoprotein, such as protein tyrosine phosphatase (PTP) activity.~~

~~9~~1. ~~A~~ Use of PRL3, or a variant, homologue, derivative or fragment thereof in the manufacture of a medicament for use in a method of treating or ~~prevention~~ preventing ~~of~~ cancer~~, such as metastatic cancer,~~ in ~~an~~ a human individual suffering or suspected to be suffering from cancer, the method comprising administering a therapeutically or prophylactically effective amount of ~~an intracellular oncoprotein~~PRL3, or a variant, homologue, derivative or fragment thereof to the individual.

2. Use according to claim 1 wherein the cancer is metastatic cancer.

3. Use according to claim 1 or claim 2 wherein medicament is a cancer vaccine.

4. Use according to any preceding claim, in which the variant, homologue, derivative or fragment of PRL3 is a polypeptide which is at least 90% identical to PRL3.

5. Use according to claim 4, in which the variant, homologue, derivative or fragment of PRL3 is a polypeptide which is at least 95% identical to PRL3.

~~10. A method according to any preceding claim, in which the intracellular oncoprotein does not comprise an extracellular domain or a transmembrane domain.~~

~~11. A method according to any preceding claim, in which the intracellular oncoprotein comprises a cytoplasmic or nuclear oncoprotein.~~

~~12~~6. A method according to any preceding claim, in which the cancer is associated with or caused by over-expression of ~~the intracellular oncoprotein~~PRL3.

~~13~~7. Use~~A method~~ according to any preceding claim, in which the cancer is selected from the group consisting of: acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical cancer, anal cancer, bladder cancer, blood cancer, bone cancer, brain tumor, breast cancer, cancer of the female genital system, cancer of the male genital system, central nervous system lymphoma, cervical cancer, childhood rhabdomyosarcoma, childhood sarcoma, chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), colon and rectal cancer, colon cancer, endometrial cancer, endometrial sarcoma, esophageal cancer, eye cancer, gallbladder cancer, gastric cancer, gastrointestinal tract cancer, hairy cell leukemia, head and neck cancer, hepatocellular cancer, Hodgkin's disease, hypopharyngeal cancer, Kaposi's sarcoma, kidney cancer, laryngeal cancer, leukemia, leukemia, liver cancer, lung cancer, malignant fibrous histiocytoma, malignant thymoma, melanoma, mesothelioma, multiple myeloma, myeloma, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, nervous system cancer, neuroblastoma, non-Hodgkin's lymphoma, oral cavity cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pituitary tumor, plasma cell neoplasm, primary CNS lymphoma, prostate cancer, rectal cancer, respiratory system, retinoblastoma, salivary gland cancer, skin cancer, small intestine cancer, soft tissue sarcoma, stomach cancer, stomach cancer, testicular cancer, thyroid cancer, urinary system cancer, uterine sarcoma, vaginal cancer, vascular system, Waldenstrom's macroglobulinemia and Wilms' tumor.

~~14. A method according to any preceding claim, in which the cancer is a metastatic cancer.~~

~~15~~8. ~~A method~~Use according to any preceding claim, in which the number of metastatic tumours in a treated individual is reduced by at least 50%, at least 60%, at least 70%, at least 80% or at least 90%, compared to an untreated individual.

~~16. An antibody capable of binding to an intracellular oncoprotein for use in a method of treatment of cancer, such as metastatic cancer, the method comprising administering a therapeutically effective amount of the antibody capable of binding to an intracellular oncoprotein to an individual suffering or suspected to be suffering from cancer.~~

~~17. An intracellular oncoprotein, or a variant, homologue, derivative or fragment thereof, for use in a method of prevention of cancer, such as metastatic cancer, the method comprising administering a prophylactically effective amount of an intracellular oncoprotein, variant, homologue, derivative or fragment thereof, to an individual suffering or suspected to be suffering from cancer.~~

~~18~~9. A pharmaceutical composition comprising ~~(a) an intracellular oncoprotein~~PRL3, or a variant, homologue, derivative or fragment thereof~~ or (b) an antibody capable of binding to an intracellular oncoprotein,~~ together with a pharmaceutically acceptable excipient, diluent or carrier.

~~19. A method, antibody, intracellular oncoprotein or pharmaceutical composition as hereinbefore described with reference to and as shown in Figures 1 to 8 of the accompanying drawings.~~