absence of modification, antibodies (including monoclonal antibodies) are only generally suitable for targeting cancer antigens located at the surface or exterior of host cells [14-15]. In the examples above, HER2 receptor is located on the cell surface and is hence accessible for antibody binding by Herceptin, Likewise, VEGF is secreted into the bloodstream and is able to be bound by Bevacizumab.

Most oncogenic proteins are intracellular proteins (such as intracellular phosphatases, intracellular kinases, transcription factors, etc), and have remained under-explored by the approach of antibody therapies. The long held view that antibodies are too large to penetrate cell membrane has hampered the technology of antibody therapy used in targeting intracellular proteins.

There is therefore an urgent need for effective ways of treating and preventing cancer metastasis. Antibodies have not hitherto been used for targeting intracellular antigens or cancer markers because of the inability of the antibodies to cross the cell membrane and the consequent inaccessibility of the antigen.

Summary

In a first aspect, there is provided use of PRL3 or a polypeptide having at least 95% sequence identity to PRL3 in the manufacture of a medicament for use in a method of treating or preventing a PRL3 expressing cancer in a human individual suffering or suspected to be suffering from a PRL3 expressing cancer, the method comprising administering a therapeutically or prophylactically effective amount of PRL3 or a polypeptide having at least 95% identity to PRL3 to the individual.

In a second aspect, there is provided a pharmaceutical composition comprising PRL3, or a polypeptide having at least 95% identity to PRL3 together with a pharmaceutically acceptable excipient, diluent or carrier.

We demonstrate in the Examples that *intracellular* oncoproteins can be targeted with either antibody therapy or vaccination to prevent cancer metastasis in mice.

Firstly, wild-type C57BL6 mice intravenously (i.v.) injected either with B16F0 or B16F10 melanoma cells, followed by i.v. injection with PRL-3 monoclonal antibody (mAb) showed that PRL-3 mAb can reduce tumors formed by B16F0 melanoma cells that express endogenous PRL-3 intracellular phosphatase, but not those by B I6F10 melanoma cells that do not express PRL-3.

Secondly, C57BL6 mice i.v. injected with either EGFP-B16F0 or EGFP-B16F10 cells in which both cell lines were engineered to overexpress EGFP, followed by i.v. injection with EGFP monoclonal antibody showed that regardless of PRL-3 expression status, EGFP mAb could eradicate tumors formed by both EGFP-B16F0 and EGFP-B16F10 melanoma cell lines.

Thirdly, polyomavirus middle T (Py-mT)-transgenic young females i.v. injected with mT antibody showed that the mT antibody could effectively reduce the formation of mT-expressing breast tumors,

It was further shown that immunisation with VHZ protein can protect against cancer development.

Therefore the disclosure provides for methods of treating cancers and metastases thereof with antibodies against intracellular oncoproteins.

In one example, there is provided use of an antibody therapy for targeting intracellular oncoproteins or proteins to prevent cancer metastasis. The antibody therapy may be an intracellular antibody therapy.

There is provided, in another example, use of an vaccine therapy comprising an oncoprotein protein for vaccination to stimulate a host to produce its own antibodies to prevent tumor formation.

The vaccine therapy may be an intracellular vaccine therapy.

In another example, there is provided 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.

The antibody may be capable of binding to an intracellular oncoprotein, preferably by being capable of crossing the plasma membrane of a cell. The antibody may comprise a monoclonal antibody or a humanised antibody. The antibody may be capable of binding to and inhibiting a biological activity of the intracellular oncoprotein, such as protein tyrosine phosphatase (PIP) activity.

Logically, by using antigen to stimulate host immune system for own antibody production, one would expect to have similar antibody therapy impact in controlling tumor progression.

C57BL6 mice vaccinated with PRL-3 or EGFP antigens showed significantly reduction in the formation of metastatic tumors expressing either PRL-3 or EGFP protein respectively, as compared with un-immunized mice. Furthermore, Py-mT mice vaccinated with mT antigen significantly prevented tumor formation in mammary glands. The results obtained from 194 wild type mice demonstrate that cancer metastasis caused by intracellular oncoproteins can be successfully blocked with antibody therapy and vaccination.

There is also provided methods of preventing cancers and metastases thereof by vaccination using intracellular oncoproteins.

There is also provided a method of prevention of cancer, .such as metastatic cancer, in an individual suffering or suspected to be suffering from cancer, the method comprising administering a prophylactically effective amount of an intracellular oncoprotein, or a variant, homologue, derivative or fragment thereof to the individual.

The intracellular oncoprotein may be such that it does not comprise an extracellular domain or a transmembrane domain. The intracellular oncoprotein may comprise a cytoplasmic or nuclear oncoprotein. The intracellular oncoprotein may comprise PRL-3 protein or polyomavirus middle T (Py-mT) protein.

The cancer may be associated with or caused by over-expression of the intracellular oncoprotein. The cancer may be selected from the group consisting of: ovarian cancer, breast cancer, liver cancer, pancreatic cancer, prostate cancer, gastric cancer, lung cancer, penis cancer, cervical cancer, brain cancer, esophageal cancer, bladder carcinoma, kidney renal cell carcinoma, ovary lymphoma and skin melanoma.

The cancer may comprise a metastatic cancer. The method may be such that 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.

In another example, there is provided 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.

In another example, there is provided 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.

In another example, there is provided a pharmaceutical composition comprising (a) an intracellular oncoprotein, 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.

The practice of the present disclosure will employ, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA and immunology, which are within the capabilities of a person of ordinary skill in the art. Such techniques are explained in the literature. See, for example, J. Sambrook, E. F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual,* Second Edition, Books 1-3, Cold Spring Harbor Laboratory Press; Ausubel, F. M. et al. (1995 and periodic supplements; *Current Protocols in Molecular Biology,* ch. 9, 13, and 16, John Wiley & Sons, New York, N.Y.); B. Roe, Wiley & Sons; J. M. Polak and James O'D. McGee, 1990, *In Situ Hybridization: Principles and Practice;* Oxford University Press; M. J. Gait (Editor), 1984, *Oligonucleotide Synthesis: A*

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. 1 by Edward Harlow, David Lane, Ed Harlow (1999, Cold Spring Harbor Laboratory Press, ISBN 0-87969544-7); 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 Roskarns and Linda Rodgers, 2002, Cold Spring Harbor Laboratory, ISBN 0-87969-630-3.

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 B1 6F0 and BI6F10 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 I x10^6 BI6F0 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' BI6F0 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 B16F1 0 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 BI6F0 cells. No difference in