CLAIMS

1. An antibody capable of binding to an PRL-1 or PRL-3 polypeptide, in which the antibody is capable of binding to an epitope bound by antibody 269, antibody 223 or antibody 318, or a variant, homologue, derivative or fragment thereof.

2. An antibody according to Claim 1, in which the antibody is capable of binding to an epitope on a PRL-1 polypeptide bound by antibody 269.

3. An antibody according to Claim 1 or 2, in which the antibody comprises an anti-PRL1 antibody capable of binding to an epitope TYKNMR or TLNKFI, or both, or a variant, homologue, derivative or fragment thereof.

4. An antibody according to Claim 1, in which the antibody is capable of binding to an epitope on a PRL-3 polypeptide bound by antibody 223 or antibody 318.

5. An antibody according to Claim 1 or 4, in which the antibody comprises an anti-PRL3 antibody capable of binding to an epitope KAKFYN or HTHKTR, or both, or a variant, homologue, derivative or fragment thereof.

6. An antibody according to any preceding claim, in which the antibody comprises the variable region of monoclonal antibody 269 (SEQ ID NO: 2, SEQ ID NO: 4), the variable region of monoclonal antibody 223 (SEQ ID NO: 6, SEQ ID NO: 8) or the variable region of monoclonal antibody 318 (SEQ ID NO: 10, SEQ ID NO: 12).

7. An antibody comprising the variable region of monoclonal antibody 269 (SEQ ID NO: 2, SEQ ID NO: 4), or a variant, homologue, derivative or fragment thereof which is capable of binding PRL-1.

8. An antibody comprising the variable region of monoclonal antibody 223 (SEQ ID NO: 6, SEQ ID NO: 8), or a variant, homologue, derivative or fragment thereof which is capable of binding PRL-1.

9. An antibody comprising the variable region of monoclonal antibody 318 (SEQ ID NO: 10, SEQ ID NO: 12), or a variant, homologue, derivative or fragment thereof which is capable of binding PRL-3.

10. An antibody according to any preceding claim which is capable of binding to an intracellular PRL-1 or PRL-3 polypeptide, preferably by being capable of crossing the plasma membrane of a cell.

11. An antibody according to any preceding claim, in which the antibody is capable of binding to and inhibiting a biological activity of PRL-1 or PRL-3, preferably protein tyrosine phosphatase (PTP) activity.

12. An antibody according to any preceding claim, in which the antibody is capable of preventing metastasis of a cancer, preferably colorectal cancer, 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.

13. An antibody according to Claim 12, in which the cancer is a PRL-1 or PRL-3 expressing cancer.

14. An antibody according to any preceding claim which is a monoclonal antibody or a humanised monoclonal antibody.

15. A combination comprising an anti-PRL-1 antibody and an anti-PRL-3 antibody, each according to any preceding claim.

16. A pharmaceutical composition comprising an antibody or combination according to any preceding claim, together with a pharmaceutically acceptable excipient, diluent or carrier.

17. An antibody capable of binding to PRL-1 or PRL-3, preferably an antibody according to any of Claims 1 to 14, a combination according to Claim 15 or a pharmaceutical composition according to Claim 16 for use in a method of treatment or prevention of cancer or metastasis thereof.

18. An antibody, combination according or composition according to Claim 17 for a use as specified therein, in which the method comprises exposing a cancer cell to the antibody or combination.

19. An antibody or combination or composition according to Claim 17 or 18 for a use as specified therein, in which the method comprises administering a therapeutically effective amount of the antibody, combination or composition to an individual suffering or suspected of suffering from cancer.

20. An antibody or combination or composition according to Claim 17, 18 or 19 for a use as specified therein, in which the cancer is a metastatic cancer, preferably a PRL-1 or PRL-3 expressing cancer.

21. An antibody or combination according to any of Claims 17 to 20 for a use as specified therein, in which the cancer comprises colorectal cancer, 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.

22. An antibody or combination according to any of Claims 17 to 21 for a use as specified therein, 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.

23. An antibody according to any of Claims 1 to 14, a combination according to Claim 15 or a pharmaceutical composition according to Claim 16 for use in a method of diagnosis of a cancer or metastasis thereof.

24. A diagnostic kit comprising an antibody according to any of Claims 1 to 14, a combination according to Claim 15 or a pharmaceutical composition according to Claim 16 together with instructions for use in the diagnosis of a cancer or metastasis thereof.

25. A polypeptide comprising a sequence selected from the group consisting of: SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or a variant, homologue, derivative or fragment thereof which is capable of binding PRL.

26. A nucleic acid comprising a sequence capable of encoding a molecule according to any of Claims 1 to 14, preferably selected from the group consisting of: SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9 and SEQ ID NO: 11, or a variant,

homologue, derivative or fragment thereof which is capable of encoding a polypeptide having PRL binding activity.

27. A cell comprising or transformed with a nucleic acid sequence according to Claim 26 or a descendent of such a cell.

28. A method of producing an antibody according to any of Claims 1 to 14, the method comprising providing a cell according to Claim 27 and expressing the antibody from the cell.

29. A method of diagnosis of cancer, such as metastatic cancer, in an individual, the method comprising exposing a biological sample from the individual to an antibody according to any of Claims 1 to 14 and detecting binding between the antibody and a PRL-1 or PRL-3 polypeptide.

30. A method of treatment or prevention 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 according to any of Claims 1 to 14, a combination according to Claim 15 or a composition according to Claim 16, to the individual.

31. A method according to Claim 29 or 30 which comprises a feature as set out in any of Claims 1 to 14 and 18 to 22.

32. A method of treatment or prevention of cancer, such as metastatic cancer, in an individual suffering or suspected to be suffering from cancer, the method comprising diagnosing cancer in the individual by a method according to Claim 29 or 31 and treating the individual by a method according to Claim 30 or 31.

33. A method of detecting a metastatic cell, the method comprising exposing a candidate cell to an antibody according to any of Claims 1 to 14 and detecting expression of PRL-1 or PRL-3 polypeptide by the cell.

34. A method of producing an animal model for metastatic tumours, the method comprising:

(a) administering a plurality of metastatic cancer cells, such as a PRL-1 or PRL-3 expressing cancer cells, into a first animal;

(b) allowing the cells to develop into metastatic tumours in the first animal;

(c) extracting a metastatic tumour from the first animal and deriving a cell line from the metastatic tumour; and

(d) administering a plurality of cells of the cell line into a second animal.

35. An animal model obtainable by a method according to Claim 34.

36. Use of an animal model produced by a method according to Claim 34 or as claimed in Claim 35 as a model for metastatic tumours.

37. A method comprising the steps of providing an antibody according to any of Claims 1 to 14 and allowing the antibody to bind to a PRL-1 or PRL-3 polypeptide.

38. A method according to Claim 37, in which the antibody is allowed to bind to a cell expressing a PRL-1 polypeptide or a PRL-3 polypeptide.

39. A method according to Claim 37 or 38, in which the PRL-1 comprises an intracellular PRL-1 polypeptide or in which the PRL-3 polypeptide comprises an intracellular PRL-3 polypeptide.

40. An antibody, combination, pharmaceutical composition, diagnostic kit, nucleic acid, cell, method or use as hereinbefore described with reference to and as shown in Figures 1 to 11 of the accompanying drawings.

CLAIMS

1. Use of an anti-PRL-1 or anti-PRL-3 antibody in the manufacture of a medicament for treating or preventing cancer or metastasis thereof, the use involving targeting intracellular PRL-1 or intracellular PRL-3 with the antibodies to ablate cancer cells and cancer metastasis.

2. The use according to claim 1 wherein the antibody is selected from the group comprising:

(a) an antibody which binds to PRL-1 comprising a heavy chain variable region sequence comprising SEQ ID NO: 2 and a light chain variable region sequence comprising SEQ ID NO: 4;

(b) an antibody which binds to PRL-3 comprising a heavy chain variable region sequence comprising SEQ ID NO: 6 and a light chain variable region sequence comprising SEQ ID NO: 8;

(c) an antibody which binds to PRL-3 comprising a heavy chain variable region sequence comprising SEQ ID NO: 10 and a light chain variable region sequence comprising SEQ IDNO: 12;

(d) an antigen binding fragment of (a), (b) or (c) which is capable of binding to an intracellular PRL-1 or PRL-3 polypeptide; and

(e) an antibody comprising a sequence which is at least 90% identical to (a), (b) or (c) and which is capable of binding to an intracellular PRL-1 or PRL-3 polypeptide.

3. Use of a nucleic acid which encodes an antibody as defined in claim 1 or claim 2 in the manufacture of a medicament for the use defined in claim 1 or claim 2.

4. The use according to Claim 3, which is selected from the group consisting of:

(a) a nucleic acid encoding an antibody (a) as defined in Claim 1 and which comprises a sequence SEQ ID NO: 1 and a sequence SEQ ID NO: 3;

(b) a nucleic acid encoding an antibody (b) as defined in Claim 1 and which comprises a sequence SEQ ID NO: 5 and a sequence SEQ ID NO: 7; and

(c) a nucleic acid encoding an antibody (c) as defined in Claim 1 and which comprises a sequence SEQ ID NO: 9 and a sequence SEQ ID NO: 11.

5. The use according to any preceding claim, in which the antibody binds to and inhibits a protein tyrosine phosphatase (PTP) activity of PRL-1 or PRL-3.

6. The use according to any preceding claim wherein the antibody comprises a monoclonal antibody or a humanised monoclonal antibody.

7. Use of a combination comprising an antibody which binds to PRL-1 and an antibody which binds to PRL-3, each according to the definition in any one of claims 1, 2, 5 or 6, in the manufacture of a medicament for treating or preventing cancer or metastasis thereof.

8. Use of a composition comprising an antibody as defined in any one of claims 1, 2, 5 or 6 or a combination as defined in Claim 7, together with a pharmaceutically acceptable excipient, diluent or carrier, in the manufacture of a medicament for treating or preventing cancer or metastasis thereof.

9. The use according to any preceding claim in which the use comprises administration of a therapeutically effective amount of the antibody, combination or composition to an individual suffering or suspected of suffering from cancer.

10. The use according to any preceding claim, in which the cancer comprises a PRL-1 or PRL-3 expressing cancer, a metastatic cancer, colorectal cancer, 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.