

over-expressed in cancers of the hepato-biliary system, pancreas and gastrointestinal tract, while its natural form, di-sialyl-Lewis^a which has an extra sialic acid sugar, is found in non-malignant epithelial cells. Expression of sialyl-Lewis^a was found to increase metastatic potential in pancreatic adenocarcinoma (16, 27) and colon cancer (14, 15). In pancreatic and colon cancer, sialyl-Lewis^a is also used as a tumour marker to monitor responses to therapy (13,17,18). Sialyl-di-Lewis^a (this has the single sialic acid found in cancers but also has the Lewis' duplicated and is only found on proteins), is expressed by a wide range of pancreatic tumours but has a very restricted normal tissue expression. More recently, human sialyl-Lewis^a mAbs were produced using a patient vaccination strategy that showed specific binding to sialyl-Lewis^a and exhibited ADCC, CDC and anti-tumour activity in a xenograft model (20). One of these mabs, 5B1, is a human IgG1 which predominantly binds Sialyl Lewis' whether the neuraminic acid is endogenously produced (N-acetyl-neuraminic acid) or exogenously derived (N-glycolyl-neuraminic acid) and whether it is on a long or short spacer. Binding to Sialyl-di-lewis^a or Sialyl lewis^{a-x} is weak and insignificant. The second mab 7E3 is a human IgM which binds equally to Sialyl lewis^a whether the neuraminic acid is endogenously produced (N acetyl neuraminic acid) or exogenously derived (N-glycolyl-neuraminic acid) and whether it is on a long or short spacer, and to Sialyl-di-lewis^a or Sialyl lewis^{a-x}. Such anti-Sialyl Lewis^a mabs would have an unacceptable normal distribution, which is supported by the observation that GivaRex (a mouse monoclonal antibody) and its patent (W00191792) has been abandoned in preclinical studies.

An aim of the present invention is to provide an improved binding member for sialyl-di- Lewis^a

In one aspect of the invention, there is provided an isolated specific binding member capable of binding sialyl-di-Lewis^a.

In another aspect of the invention, there is provided a binding member which competes for binding to the same epitope as a binding member as described herein, and optionally wherein the binding member is in the same form as the binding member as described herein.

In another aspect of the invention, there is provided a binding member as described herein for use as a medicament.

In another aspect of the invention, there is provided a binding member as described herein for use in the prevention, treatment or diagnosis of cancer.

In another aspect of the invention, there is provided a use of a binding member as described herein in the manufacture of a medicament for treating or preventing cancer, wherein the medicament is to be administered to a subject in need of thereof.

In another aspect of the invention, there is provided a nucleic acid comprising a sequence encoding a binding member as described herein.

In another aspect of the invention, there is provided a recombinant host cell which comprises the nucleic acid as described herein.

In another aspect of the invention, there is provided a method for diagnosis of cancer comprising using a binding member as describe herein to detect the glycans sialyl-di-Lewis^a and sialyl-Lewis^{a-x} and/or mono-sialyl-Lewis^a only attached to a glycoprotein in a sample obtained from an individual.

In another aspect of the invention, there is provided a pharmaceutical composition comprising the binding member as described herein, and a pharmaceutically acceptable carrier.

According to a first aspect of the invention, there is provided an isolated specific binding member capable of binding sialyl-di-Lewis^a.

The binding member may be specific for sialyl-di-Lewis^a. In one embodiment, the binding member may be specific for sialyl-di-Lewis^a and sialyl-Lewis^{a-x}. The binding member may be specific for sialyl-di-Lewis^a. In one embodiment, the binding member may be specific for sialyl-di-Lewis^a and sialyl-Lewis^{a-x} present in tumour tissue. The binding member may not bind, or may not significantly bind, mono-sialyl-Lewis^a bound to a glycolipid. Additionally or alternatively, the binding member may not bind, or may not significantly bind, di-sialyl-

17. The binding member according to any of claims 1 to 15, wherein the binding member is an scFv comprising, in the following order, 1) leader sequence, 2) light chain variable region, 3) 3x GGGGS spacer, and 4) heavy chain variable region, optionally further comprising either 5' or 3' purification tags.
18. The binding member according to any preceding claim, wherein the binding member is provided in the form of a chimeric antigen receptor (CAR).
19. The binding member according to claim 18, wherein the binding member is an scFv provided in the form of a chimeric antigen receptor (CAR) either in the heavy chain-light chain orientation or the light chain-heavy chain orientation.
20. The binding member according to any preceding claim, wherein the binding member is monoclonal, such as a monoclonal antibody.
21. The binding member according to any preceding claim, wherein the binding member is a human, humanised, chimeric or veneered antibody.
22. The binding member according to any preceding claim, wherein the binding member is a drug conjugate, such as an antibody-drug conjugate (ADC).
23. A binding member which competes for binding to the same epitope as a binding member according to any one of claims 1 to 22, and optionally wherein the binding member is in the same form as the binding member according to any of claims 1 to 22.
24. A binding member according to any preceding claim, for use as a medicament.
25. A binding member according to any of claims 1 to 23, for use in the prevention, treatment or diagnosis of cancer.
25. Use of a binding member according to any of claims 1 to 23 in the manufacture of a medicament for treating or preventing cancer, wherein the medicament is to be administered to a subject in need of thereof.

27. The binding member for the use of claims 24 or 25, or the use of claim 26, wherein the cancer is colorectal cancer, gastric cancer, pancreatic cancer, lung cancer, ovarian cancer or breast cancer.
28. The binding member for the use of claims 24, 25 or 27, or the use of claim 26 or claim 27, wherein the binding member is to be administered, or arranged to be administered, alone or in combination with other treatments.
29. A nucleic acid comprising a sequence encoding a binding member according to any of claims 1-23.
30. The nucleic acid according to claim 29, wherein the nucleic acid is a construct in the form of a plasmid, vector, transcription or expression cassette.
31. A recombinant host cell which comprises the nucleic acid according to claim 29 or claim 30.
32. A method for diagnosis of cancer comprising using a binding member as claimed in any of claims 2 to 23 to detect the glycans sialyl-di-Lewis^a and sialyl-Lewie^{a-x} and/or mono-sialyl-Lewis^a only attached to a glycoprotein in a sample obtained from an individual.
33. The method according to claim 32, wherein the pattern of glycans detected by the binding member is used to stratify therapy options for the individual.
34. A pharmaceutical composition comprising the binding member according to any of claims 1 to 23, and a pharmaceutically acceptable carrier.
35. The pharmaceutical composition according to claim 34, further comprising at least one other pharmaceutical active.