

SUMMARY

In one example, the present disclosure provides a protein that binds an extracellular part of a membrane associated member of: the epidermal growth
5 factor (EGF) receptor family or cMET; and an extracellular part of a membrane associated member of a WNT signaling pathway.

In one aspect, the present disclosure refers to a bispecific antibody or a functional part comprising the antigen binding parts thereof, that comprises a variable domain that binds an extracellular part of epidermal growth factor (EGF)
10 receptor (EGFR), and a variable domain that binds an extracellular part of leucine-rich repeat-containing G-protein coupled receptor 5 (LGR5).

In another aspect, the present disclosure refers to the bispecific antibody or functional part thereof as disclosed herein, for use in the treatment of an individual that has cancer.

15 In yet another aspect, the present disclosure refers to use of the bispecific antibody or functional part thereof disclosed herein, in the manufacture of a medicament for treating cancer.

In yet another aspect, the present disclosure refers to a cell system comprising the bispecific antibody or functional part thereof disclosed herein, and a
20 cell that expresses the epidermal growth factor receptor EGFR and that expresses LGR5.

In yet another aspect, the present disclosure refers to an *in vitro* method for inhibiting proliferation of a cell that expresses the epidermal growth factor (EGF) receptor EGFR and that expresses LGR5, a membrane associated member of the
25 WNT pathway in a system permissive for proliferation of the cell, the method comprising providing the system with the bispecific antibody disclosed herein.

Claims

1. A bispecific antibody or a functional part comprising the antigen binding
5 parts thereof, that comprises a variable domain that binds an extracellular part of epidermal growth factor (EGF) receptor (EGFR), and a variable domain that binds an extracellular part of leucine-rich repeat-containing G-protein coupled receptor 5 (LGR5).
- 10 2. The bispecific antibody or functional part thereof of claim 1, comprising a variable domain that binds EGFR and a variable domain that binds LGR5
 - wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequence of VH chain MF3370, MF3755, MF4280 or MF4289 as depicted in Figure 1; and
 - 15 - wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of VH chain MF5790; MF5803; MF5805; MF5808; MF5809; MF5814; MF5816; MF5817; or MF5818 as depicted in Figure 1.
- 20 3. The bispecific antibody or functional part thereof of claims 1 or 2, comprising a variable domain that binds EGFR and a variable domain that binds LGR5
 - wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequence of VH chain MF3370 as depicted in Figure 1; and
 - wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of VH chain MF5790 as depicted in Figure 1.
- 25 4. The bispecific antibody or functional part thereof of claims 1 or 2, comprising a variable domain that binds EGFR and a variable domain that binds LGR5
 - wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequence of VH chain MF3755 as depicted in Figure 1; and
 - 30 - wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of VH chain MF5816 as depicted in Figure 1.
5. The bispecific antibody or functional part thereof of claims 1 or 2, comprising a variable domain that binds EGFR and a variable domain that binds LGR5

- wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequence of VH chain MF4280 as depicted in Figure 1; and

- wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of VH chain MF5814 as depicted in Figure 1.

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6. The bispecific antibody or functional part thereof of claims 1 or 2, comprising a variable domain that binds EGFR and a variable domain that binds LGR5

- wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequence of VH chain MF4280 as depicted in Figure 1; and

10 - wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of VH chain MF5818 as depicted in Figure 1.

7. The bispecific antibody or functional part thereof according to any one of the preceding claims, for use in the treatment of an individual that has cancer.

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8. Use of the bispecific antibody or functional part thereof according to any one of claims 1-6, in the manufacture of a medicament for treating cancer.

20 9. The use according to claim 8, wherein the cancer is an adenocarcinoma.

10. The use according to claim 8, wherein the cancer is Colorectal cancer; Pancreatic cancer; Lung cancer; Breast cancer; Liver cancer; Prostate cancer; Ovarian cancer; Cervical cancer; Endometrial cancer; Head and Neck cancer; Melanoma; Testis cancer; Urothelial cancer; Renal cancer; Stomach cancer; or Carcinoid cancer.

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11. The use according to claim 8, wherein the cancer is Colorectal cancer.

30 12. A cell system comprising the bispecific antibody or functional part thereof according any of the preceding claims, and a cell that expresses the epidermal growth factor receptor EGFR and that expresses LGR5.

13. An *in vitro* method for inhibiting proliferation of a cell that expresses the epidermal growth factor (EGF) receptor EGFR and that expresses LGF5, a membrane associated member of the WNT pathway in a system permissive for proliferation of the cell, the method comprising providing the system with the
- 5 bispecific antibody according to any one of claim 1-6.