

Claims

1. A bispecific antibody or a functional part comprising the antigen binding parts thereof, that comprises a variable domain that binds epidermal growth factor (EGF) receptor (EGFR), and a variable domain that binds leucine-rich repeat-containing G-protein coupled receptor 5 (LGR5),
- wherein the VH chain of the variable domain that binds EGFR comprises the CDR1, CDR2 and CDR3 sequences of the VH chains MF3370, MF3755, MF4280 or MF4289 as depicted in Figure 1; and
- wherein the VH chain of the variable domain that binds LGR5 comprises the CDR1, CDR2 and CDR3 sequences of the VH chains MF5790; MF5803; MF5805; MF5808; MF5809; MF5814; MF5816; MF5817; or MF5818 as depicted in Figure 1.
2. The bispecific antibody or functional part thereof of claim 1, wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequences of the VH chains MF3370, MF3755, MF4280 or MF4289 as depicted in Figure 1; and wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequences of the VH chains MF5790; MF5803; MF5805; MF5808; MF5809; MF5814; MF5816; MF5817; or MF5818 as depicted in Figure 1.
3. The bispecific antibody or functional part thereof of claim 1, wherein the VH chain of the variable domain that binds EGFR comprises the CDR1, CDR2 and CDR3 sequences of the VH chain MF3755 as depicted in Figure 1; and wherein the VH chain of the variable domain that binds LGR5 comprises the CDR1, CDR2 and CDR3 sequences of the VH chain MF5816 as depicted in Figure 1.
4. The bispecific antibody or functional part thereof of claim 1 or 2, wherein the VH chain of the variable domain that binds EGFR comprises the amino acid sequences of the VH chain MF3755 as depicted in Figure 1; and wherein the VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of the VH chain MF5816 as depicted in Figure 1.

5. The bispecific antibody or functional part thereof of any one of the preceding claims, wherein both variable domains comprise a VL chain which comprises the CDR1, CDR2 and CDR3 amino acid sequences of the VL chain as depicted in Figure 3.
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6. The bispecific antibody or functional part thereof of any one of the preceding claims, wherein both variable domains comprise a VL chain which comprises the CDR1, CDR2 and CDR3 amino acid sequences QSISSY, AAS, and QQSYSTPPT, respectively, of the VL chain as depicted in Figure 3.
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7. The bispecific antibody or functional part thereof of any one of the preceding claims, wherein both variable domains comprise a VL chain which comprises the amino acid sequences of the VL chain as depicted in Figure 3.
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8. A bispecific antibody comprising a variable domain that can bind an epitope on Leucine Rich Repeat Containing G Protein-Coupled Receptor 5 (LGR5), which epitope is located within amino acid residues 21-118 of SEQ ID NO: 1, of which amino acid residues D43; G44, M46, F67, G90, and F91 are involved in binding of the antibody to the epitope; and a variable domain that can bind an epitope on
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- human EGFR of which amino acid residues I462; G465; K489; I491; N493; and C499 of SEQ ID NO:2 are involved in binding of the antibody to the epitope.
9. The bispecific antibody of claim 8, wherein one or more of the amino acid residue substitutions of D43A; G44A, M46A, F67A, G90A, and F91A reduces the
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- binding of the antibody of LGR5.
10. The bispecific antibody of claim 8 or 9, wherein the epitopes for LGR5 and EGFR are determined using shotgun mutagenesis.
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11. The bispecific antibody of any one of claims 8-10, wherein the epitope on LGR5 is a conformational epitope.

12. The bispecific antibody of any one of claims 8-11, wherein one or more of the amino acid residue substitutions selected from I462A; G465A; K489A; I491A; N493A; and C499A reduce the binding of the antibody to human EGFR.
- 5 13. 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.
14. Use of the bispecific antibody or functional part thereof according to any one of the preceding claims, in the manufacture of a medicament for treating cancer.
- 10 15. The use according to claim 13 or 14, wherein the cancer is an adenocarcinoma.
16. The use according to claim 13 or 14, wherein the cancer is Colorectal cancer;
- 15 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.
- 20 17. The use according to claim 13 or 14, wherein the cancer is Colorectal cancer.
18. The use according to claim 13 or 14, wherein the cancer is Head and Neck cancer.
- 25 19. A cell system comprising the bispecific antibody or functional part thereof according to any one of claims 1-12, and a cell that expresses the epidermal growth factor receptor (EGFR) and that expresses LGR5.
20. An *in vitro* method for inhibiting proliferation of a cell that expresses the
- 30 epidermal growth factor (EGF) receptor (EGFR) and that expresses LGR5, 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 bispecific antibody according to any one of claims 1-12.