certain embodiments, the antibodies, or antigen binding portions thereof, inhibit tumor growth by at least about 80% in an *in vivo* human non-small-cell lung carcinoma (NSCLC) xenograft assay relative to a human IgG antibody which is not specific for EGFR.

In some embodiments, the antibodies, or antigen binding portions thereof, comprise a heavy chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a heavy chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a heavy chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10; and a light chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a light chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a light chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6. In yet another embodiment, the antibodies, or antigen binding portions thereof, comprise a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5. In other embodiments, the antibodies, or antigen binding portions thereof, comprise a heavy chain constant region comprising the amino acid sequence set forth in SEQ ID NO: 41 and/or a light chain constant region comprising the amino acid sequence set forth in SEQ ID NO: 43. In a further embodiment, the antibodies, or antigen binding portions thereof, comprise a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 15, and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 13. In another embodiment, the the antibodies, or antigen binding portions thereof, are conjugated to an auristatin.

In one embodiment, the invention features an anti-human epidermal growth factor receptor (anti-hEGFR) antibody comprising a heavy chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a heavy chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a heavy chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10; and a light chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a light chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a light chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6, wherein the antibody is an IgG isotype.

In one embodiment, the invention features an antibody drug conjugate (ADC) comprising an anti-human epidermal growth factor receptor (anti-hEGFR) antibody conjugated to at least one auristatin, wherein the anti-hEGFR antibody is an IgG isotype and comprises a heavy chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10; and a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6.

The invention also provides, in certain embodiments, isolated nucleic acids encoding an antibodies, or antigen binding portions thereof, like that described herein.

The invention also includes, in certain embodiments, anti-hEGFR antibodies, or antigen binding portions thereof, comprising a light chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 40, a light chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 39, and a light chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 38; and a heavy chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 37, a heavy chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 36, and a heavy chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 35.

In certain embodiments, the invention features anti-hEGFR antibodies, or antigen binding portions thereof, comprising a heavy chain variable region comprising an amino acid sequence selected from the group consisting of 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, and 78; and a light chain variable region comprising an amino acid sequence selected from the group consisting of 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, and 79.

In other embodiments, the invention includes anti-hEGFR antibodies, or antigen binding portions thereof, comprising a heavy chain CDR set (CDR1, CDR2, and CDR3) selected from the group consisting of SEQ ID NOs: 10, 11, and 12; SEQ ID NOs: 16, 17, and 18; SEQ ID NOs: 10, 11,

CLAIMS

1. An anti-human epidermal growth factor receptor (anti-hEGFR) antibody comprising

a heavy chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a heavy chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a heavy chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10; and

a light chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a light chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a light chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6,

wherein the antibody is an IgG isotype.

2. The antibody of claim 1, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5.

3. The antibody of claim 1, comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 15, and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 13.

4. The antibody of claim 1, which is conjugated to at least one drug.

5. The antibody of claim 4, wherein the at least one drug is selected from the group consisting of a dolastatin, a maytansinoid, and a plant alkaloid.

6. An isolated nucleic acid encoding an antibody of claim 1.

7. The antibody of claim 4, wherein the at least one drug is an auristatin.

8. The antibody of claim 7, wherein the auristatin is monomethyauristatin E (MMAE).

9. The antibody of claim 7, wherein the auristatin is monomethylaurisatin F (MMAF).

10. An antibody drug conjugate (ADC) comprising an anti-human epidermal growth factor receptor (anti-hEGFR) antibody conjugated to at least one auristatin, wherein the anti-hEGFR antibody is an IgG isotype and comprises

a heavy chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10; and

a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6.

11. The ADC of claim 10, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 9, and wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 5.

12. The ADC of claim 10, wherein the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 15, and comprises a light chain comprising the amino acid sequence set forth in SEQ ID NO: 13.

13. The ADC of claim 11, wherein the antibody is an IgG1 isotype.

14. The ADC of claim 13, wherein the auristatin is monomethylauristatin E (MMAE).

15. The ADC of claim 14, wherein the antibody is conjugated to MMAE via a maleimidocaproyl, valine-citrulline linker.

16. A pharmaceutical composition comprising an ADC mixture comprising a plurality of the ADC of claim 15, and a pharmaceutically acceptable carrier.

17. The pharmaceutical composition of claim 16, wherein the ADC mixture has an average drug to antibody ratio (DAR) of 1 to 4.

18. An antibody drug conjugate (ADC) comprising an anti-EGFR IgG1 antibody covalently linked to maleimidocaproyl, valine-citrulline, p-aminobenzyloxycarbamyl-monomethylauristatin E (mc-vc-PABA-MMAE),

wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9, and comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5, and

wherein 1 to 4 molecules of MMAE are linked to the antibody.

19. The ADC of claim 18, wherein the antibody comprises a heavy chain comprising the

amino acid sequence set forth in SEQ ID NO: 15, and comprises a light chain comprising the amino acid sequence set forth in SEQ ID NO: 13.

20. The ADC of claim 18, wherein 2 to 4 molecules of MMAE are linked to the antibody.

21. A pharmaceutical composition comprising an ADC mixture comprising a plurality of the ADC of claim 18, and a pharmaceutically acceptable carrier.

22. The pharmaceutical composition of claim 21, wherein the ADC mixture has an average drug to antibody ratio (DAR) of 2 to 4.