ANTIBODIES OF INCREASED AFFINITY FOR THE RECEPTOR OF THE EPIDERMAL GROWTH FACTOR AND ITS DERIVED FRAGMENTS

CLAIMS

1. A recombinant monoclonal antibody (mAb) that recognizes the extracellular region of the human epidermal growth factor receptor (Her1) characterized in that it shares more than 95% identity with respect to the nimotuzumab antibody and that the CDR2 sequence of the variable region of the heavy chains are selected from the group comprising:

- SEQ ID NO. 20 and
- SEQ ID NO. 21,

the sequence of CDR1 is SEQ ID NO. 9 and the sequence of CDR3 is SEQ ID NO.3 in these heavy chains and the CDR sequences of the variable region of the light chains are:

- CDR 1 SEQ ID NO. 22
- CDR 2 SEQ ID NO. 23
- CDR 3 SEQ ID NO. 24.

2. An mAb that recognizes the Her1 characterized in that the CDR2 sequence of the variable region of the heavy chains is selected from the group comprising:

- SEQ ID NO. 10,

- SEQ ID NO. 11,
- SEQ ID NO. 12,
- SEQ ID NO. 17,
- SEQ ID NO. 18 and
- SEQ ID NO. 29,

the sequence of CDR1 is SEQ ID NO. 9 and the sequence of CDR3 is SEQ ID NO.3, these heavy chains and the CDR sequences of the variable region of the light chains are:

- CDR 1 SEQ ID NO. 22
- CDR 2 SEQ ID NO. 23
- CDR 3 SEQ ID NO. 24.

3. An mAb that recognizes Her1 characterized in that the CDR2 sequence of the variable region of the heavy chains is selected from the group comprising:

- SEQ ID NO. 2 and
- SEQ ID NO. 8,

the sequence of CDR1 is SEQ ID NO. 1 and the sequence of the CDR3 is SEQ ID NO.3, these heavy chains and the CDR sequences of the variable region of the light chains are shown below:

- CDR 1 SEQ ID NO. 22
- CDR 2 SEQ ID NO. 23
- CDR 3 SEQ ID NO. 24.

4. An mAb that recognizes Her1 characterized in that the CDR1 sequence of the variable region of the heavy chains is selected from the group comprising:

- SEQ ID NO. 13 and
- SEQ ID NO. 19,

the CDR2 sequence is SEQ ID NO. 14 and the sequence of CDR3 is SEQ ID NO.3 these heavy chains and the CDR sequences of the variable region of the light chains are:

- CDR 1 SEQ ID NO. 22
- CDR 2 SEQ ID NO. 23
- CDR 3 SEQ ID NO. 24.

5. An mAb that recognizes the Her1 characterized because the CDR of the variable region of the heavy and light chains contains the following sequences:

Heavy chain

- CDR1 SEQ ID NO. 15
- CDR2 SEQ ID NO. 16
- CDR3 SEQ ID NO.3

Light chain

- CDR 1 SEQ ID NO. 22
- CDR 2 SEQ ID NO. 23
- CDR 3 SEQ ID NO. 24.

6. The mAb according to claims 1-5 characterized in that the framework regions (FW) of the variable region of the heavy and light chains have the following sequences:

   Heavy chain

   - FW 1 SEQ ID NO. 4
   - FW 2 SEQ ID NO. 5
   - FW 3 SEQ ID NO. 6
   - FW 4 SEQ ID NO. 7

   Light chain

   - FW 1 SEQ ID NO. 25
   - FW 2 SEQ ID NO. 26
   - FW 3 SEQ ID NO. 27
   - FW 4 SEQ ID NO. 28

7. The mAb according to claims 1 to 6, characterized in that the sequence of the heavy chain constant regions is a human IgG1.
8. The mAb according to claims 1 to 6 characterized in that the constant regions of light chain is a human kappa.
9. An antigen binding fragment derived from the mAb of claims 1-8 characterized in that it is a fragment of Fab type.
10. An antigen binding fragment according to claims 1-8 characterized in that it is a fragment of (Fab) 2 type.
11. An antigen binding fragment according to claims 1-6, characterized in that it is a single-chain variable region fragment.

12. A pharmaceutical composition useful in cancer therapy having as active ingredient the mAb or fragments of claims 1-11 in a range from 50 to 400 mg and a pharmaceutically acceptable vehicle.
13. A pharmaceutical composition useful in the diagnosis of tumors having as active ingredient the mAbs or fragments of claims 1-11 in a range from 1 to 9 mg and a pharmaceutically acceptable vehicle.
14. Use of the mAbs and fragments of claims 1-11 in the therapy of tumors expressing EGFR.
15. Use of the mAbs and fragments of claims 1-11 when they are conjugated to an appropriate marker for the invivo diagnosis of tumors bearing EGFR.
16. Use of the mAbs or fragments of claims 1-11 when they are conjugated with proteins or protein domains of immunological interest to direct the immune response against EGFR positive tumors.