as a recombinant protein in *E. Coli* is also the subject of a patent application [WO2006/015371] by Genentech. However, this molecule that could not be considered as an antibody because of its particular scarfold, displays also mutations that could be immunogenic in humans. In terms of activity, this unglycosylated molecule is devoided of effector functions and finally, no clear data demonstrate that OA5D5 inhibits dimerization of c-Met. Moreover, when tested in the G55 *in vivo* model, a glioblastoma cell line that expresses c-Met but not HGF mRNA and protein and that grows independently of the ligand, the one armed anti-c-Met had no significant effect on G55 tumor growth suggesting that OA5D5 acts primarily by blocking HGF binding and is not able to target tumors activated independently of HGF [Martens T. et al, Clin. Cancer Res., 2006, 12(20):6144-6152].

Another antibody targeting c-Met is described by Pfizer as an antibody acting "predominantly as c-Met antagonist, and in some instance as a c-Met agonist" [WO 2005/016382]. No data showing any effect of Pfizer antibodies on c-Met dimerization is described in this application.

One of the innovant aspects of the present invention is to generate mouse monoclonal antibodies without intrinsic agonist activity and inhibiting c-Met dimerization. In addition of targeting ligand-dependent tumors, this approach will also impair ligand-independent activations of c-Met due to its overexpression or mutations of the intra cellular domains which remained dependent to oligomerization for signalling. Another aspect of the activity of such antibodies could be a steric hindrance for c-Met interaction with its partners that will result in impairment of c-Met functions. These antibodies will be humanized and engineered preferentially, but not limited, as human IgG1 to get effector functions such as ADCC and CDC in addition to functions linked to the specific blockade of the c-Met receptor.

SUMMARY

In one aspect of the invention, there is provided an isolated antibody, or one of its functional divalent fragment or derivatives, characterized in that the antibody comprises a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 comprising respectively the amino acid sequences SEQ ID Nos. 56, 57 and 58; and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 comprising respectively the amino acid sequences SEQ ID Nos. 59, 60 and 61.

In another aspect, there is provided a murine hybridoma capable of secreting an antibody as defined herein, characterized in that said hybridoma is the murine hybridoma deposited at the CNCM, Institut Pasteur, Paris, on March 14, 2007 under the number I-3724.

In another aspect, there is provided an isolated nucleic acid, characterized in that it is chosen from the following nucleic acids:

a) a nucleic acid, DNA or RNA, coding for an antibody, or one of its functional divalent fragment or derivatives, as defined herein;

b) a nucleic acid comprising a DNA sequence comprising the sequences of SEQ ID No. 64, SEQ ID No. 65, SEQ ID No. 66 and the sequences of SEQ ID No. 67, SEQ ID No. 68 and SEQ ID No. 69;

c) a nucleic acid comprising a DNA sequence comprising the sequences of SEQ ID No. 70 and SEQ ID No. 71;

d) the corresponding RNA nucleic acids of the nucleic acids as defined in b) and/or c);

e) the complementary nucleic acids of the nucleic acids as defined in a), b) and c); and

f) a nucleic acid of at least 18 nucleotides capable of hybridizing under conditions of high stringency with at least one of the CDRs of SEQ ID Nos. 64 to 69.

In another aspect, there is provided a vector comprising a nucleic acid as defined herein.

In another aspect, there is provided a host cell comprising a vector as defined herein.

In another aspect, there is provided a process for production of an antibody, or one of its functional divalent fragment or derivatives, as defined herein, characterized in that the process comprises:

a) culturing a host cell as defined herein, in a medium and under appropriate culture conditions; and

b) recovering said antibodies, or one of their functional divalent fragment or derivatives from the culture medium or said cultured cells.

In another aspect, there is provided the antibody, or one of its functional divalent fragment or derivatives, as defined herein, or obtained by the process as defined herein, as a medicament.

In another aspect, there is provided a composition comprising as an active principle a compound consisting of an antibody, or one of its functional divalent fragment or derivatives, as defined herein, or obtained by the method as defined herein, or produced by hybridoma as defined herein.

In another aspect, there is provided the composition as defined herein as a medicament.

In another aspect, there is provided the use of an antibody, or one of its functional divalent fragment or derivatives, as defined herein, or obtained by the process as defined herein, or produced by the hybridoma as defined herein, or of a composition as defined herein for the preparation of a medicament to inhibit the growth and/or the proliferation of tumor cells.

In another aspect, there is provided the use of an antibody, or one of its functional divalent fragment or derivatives, as defined herein, or obtained by the process as defined herein, or produced by the hybridoma as defined herein, or of a composition as defined herein, for the preparation of a medicament for the prevention or for the treatment of cancer.

In another aspect, there is provided a method of *in vitro* diagnosis of illnesses induced by an overexpression or an underexpression of the c-Met receptor starting from a biological sample in which the abnormal presence of c-Met receptor is suspected, characterized in that said method comprises a step wherein said biological sample is contacted with the antibody, or one of its functional divalent fragment or derivatives, as defined herein, or obtained by the process as defined herein, or produced by the hybridoma as defined herein, it being possible for said antibody to be, if necessary, labeled.

DISCLOSURE OF THE INVENTION

Surprisingly, for the first time, inventors have managed to generate an antibody capable of binding to c-Met but also capable of inhibiting the c-Met dimerization. If it is true that, in the prior art, it is sometimes suggested that an antibody capable of inhibiting the dimerization of c-Met with its partners could be an interesting one, it has never been disclosed, or clearly suggested, an antibody capable of doing so. Moreover,