CLAIMS

1. An antagonist that inhibits c-met signaling activity of a human hyperstabilized c-met polypeptide, wherein the hyperstabilized c-met polypeptide comprises a deletion of at least a portion of exon 14 such that its degradation is diminished compared to wild type c-met, and wherein the hyperstabilized c-met polypeptide has c-met signaling activity.

2. The antagonist of claim 1, wherein the antagonist is an antibody that binds to an epitope formed by in-frame splicing of exon 13 and exon 15 of human c-met.

3. The antagonist of claim 1, wherein at least a portion of exon 14 of hyperstabilized c- met polypeptide is deleted.

4. The antagonist of claim 1, wherein the antagonist is an inhibitory RNA that preferentially inhibits expression from a nucleic acid molecule encoding a splice variant of c-met wherein exon 13 is spliced to exon 15.

5. The antagonist of claim 1, wherein inhibition of c-met signaling activity by the antagonist comprises enhancement of cellular degradation of the hyperstabilized c- met protein.

6. The antagonist of claim 1, wherein the antagonist is linked to a toxin.

7. The antagonist of claim 1, wherein the antagonist does not specifically bind wild type c-met polypeptide.

8. The antagonist of claim 1, wherein the antagonist does not substantially inhibit wild type c-met polypeptide activity.

9. Use of an antagonist of any of the preceding claims for the manufacture of a medicament for treating a tumor in a subject.

10. The use of claim 9, wherein the tumor is determined to comprise hyperstabilized c-met.

11. The use of claim 10, wherein the tumor is determined to comprise mutant c-met comprising deletion of at least a portion of exon 14.

12. The use of claim 9, wherein the medicament is to be administered in conjunction with an agent that induces receptor protein degradation.

CLAIMS:

1. An antagonist that inhibits c-met signaling activity of a human hyperstabilized c-met polypeptide, wherein the hyperstabilized c-met polypeptide comprises an in-frame deletion of exon 14, the deletion removing the Y1003 phosphorylation site, such that degradation of the polypeptide is diminished compared to wild type c-met, and wherein the hyperstabilized c-met polypeptide has c-met signaling activity, for use in a method of treating a tumor comprising hyperstabilized c-met in a subject, said method comprising administering said antagonist to a subject, whereby the tumor is treated, wherein the antagonist is
(i) an antibody that binds to human hyperstabilized c-met polypeptide;
or
(II) an inhibitory RNA or antisense oligonucleotide that inhibits expression from a nucleic acid molecule encoding human hyperstabilized c-met polypeptide.

2. The antagonist for use according to claim 1, wherein the tumor is a lung tumor.

3. The antagonist for use according to claim 2, wherein the tumor is a non-small cell lung cancer (NSCLC) tumor.

4. The antagonist for use according to claim 1, wherein inhibition of c-met signaling activity by the antagonist comprises enhancement of cellular degradation of the hyperstabilized c-met protein.

5. The antagonist for use according to claim 1 (i), wherein the antagonist is linked to a toxin.

6. The antagonist for use according to claim 1, wherein the antagonist does not substantially inhibit human wild type c-met polypeptide activity.

7. The antagonist for use according to claim 1, wherein the antagonist is an antibody that does not specifically bind human wild type c-met polypeptide.

8. The antagonist for use according to claim 1, wherein the antagonist is an antibody that binds to an epitope formed by in-frame splicing of exon 13 and exon 15 of human c-met.

9. The antagonist for use according to claim 1, wherein the antagonist is an inhibitory RNA or an antisense oligonucleotide that preferentially inhibits

expression from a nucleic acid molecule encoding a splice variant of c-met wherein exon 13 is spliced to exon 15.

10. The antagonist for use according to claim 1, wherein the antagonist is an antibody which is a monoclonal antibody, antibody fragment, chimeric antibody, humanized antibody, human antibody, multi-specific antibody or single-chain antibody.

11. The antagonist for use according to claim 1, wherein the method comprises administering the antagonist in conjunction with an agent that induces receptor protein degradation.

12. Use of an antagonist that inhibits c-met signaling activity of a human hyperstabilized c-met polypeptide, wherein the hyperstabilized c-met polypeptide comprises an in-frame deletion of exon 14, the deletion removing the Y1003 phosphorylation site, such that degradation of the polypeptide is diminished compared to wild type c-met, and wherein the hyperstabilized c-met polypeptide has c-met signaling activity, for the manufacture of a medicament for treating a tumor comprising hyperstabilized c-met in a subject, said medicament is to be administered to a subject, whereby the tumor is treated,
wherein the antagonist is
(i) an antibody that binds to human hyperstabilized c-met polypeptide;
or
(II) an inhibitory RNA or antisense oligonucleotide that inhibits expression from a nucleic acid molecule encoding human hyperstabilized c-met polypeptide.

13. The use according to claim 12, wherein the tumor is a lung tumor.

14. The use according to claim 13, wherein the tumor is a non-small cell lung cancer (NSCLC) tumor.

15. The use according to claim 12, wherein inhibition of c-met signaling activity by the antagonist comprises enhancement of cellular degradation of the hyperstabilized c-met protein.

16. The use according to claim 12 (i), wherein the antagonist is linked to a toxin.

17. The use according to claim 1, wherein the antagonist does not substantially inhibit human wild type c-met polypeptide activity.

18. The use according to claim 12, wherein the antagonist is an antibody that does not specifically bind human wild type c-met polypeptide.

19. The use according to claim 1, wherein the antagonist is an antibody that binds to an epitope formed by in-frame splicing of exon 13 and exon 15 of human c-met.

20. The use according to claim 12, wherein the antagonist is an

inhibitory RNA or an antisense oligonucleotide that preferentially inhibits expression from a nucleic acid molecule encoding a splice variant of c-met wherein exon 13 is spliced to exon 15.

21. The use according to claim 12, wherein the antagonist is an antibody which is a monoclonal antibody, antibody fragment, chimeric antibody, humanized antibody, human antibody, multi-specific antibody or single-chain antibody.

22. The use according to claim 12, wherein the method comprises administering the antagonist in conjunction with an agent that induces receptor protein degradation.