Claims

1. Use of an inhibitory anti-LIF antibody in the manufacture of a medicament for the treatment of cancer, wherein said cancer is selected from breast, heart, lung, small intestine, colon, spleen, bladder, head, neck, ovarian, brain, pancreatic, skin, bone, bone marrow, blood, thymus, uterine, testicular and liver tumors.

2. *In vitro* method for the identification of compounds capable of blocking/inhibiting the cell proliferation of tumor cells induced by LIF, comprising the steps of:

(i) contacting a cell expressing the receptor for LIF with LIF and a candidate compound, and

(ii) identifying those compounds blocking the cell proliferation of said cell.

3. The method according to claim 2, wherein the cell expressing the receptor for an IL-6 type cytokine is a glioma cell, preferably a glioma initiating cell (GIC).

4. *In vitro* method for the diagnosis of cancer in a subject or for determining the predisposition of a subject to suffer from cancer, or for determining the stage or severity of cancer in a subject, or for monitoring the effect of the therapy administered to a subject with cancer, or for designing a customized therapy for a patient suffering from cancer, or for selecting patients suffering from cancer, or for the prognosis of life expectancy of subjects suffering from cancer which comprises quantifying the expression levels of the gene encoding LIF or of the protein encoded by said gene in a biological sample from said subject, wherein an increase of the expression of the gene encoding LIF or of the protein encoded by said gene, with respect to the expression of the gene encoding LIF or of the protein encoded by said gene in a control sample, is indicative of a cancer, or of greater predisposition of said subject to suffer from cancer or of the non-response to the therapy administered to said subject, or wherein the patient is selected to receive treatment with an inhibitory agent of LIF.

12. An *in vitro* method for designing a customized therapy for a patient suffering from cancer according to claim 4 comprising:

(a) quantifying the expression levels of LIF in said patient, and

(b) comparing said expression levels with control levels,

wherein if the expression levels of LIF in said patient are greater than the control values, then an inhibitory agent of LIF is administered to said patient.

13. An *in vitro* method for selecting patients suffering from cancer according to claim 4, to be treated with an inhibitory agent of LIF comprising

(a) quantifying the expression levels of LIF in said patient, and

(b) comparing said expression levels with control levels,

wherein if the expression levels of LIF in said patient are greater than the control values, then said patient is selected to receive treatment with an inhibitory agent of LIF.

7. The method according to claim 4, wherein the quantification of the expression levels of the gene encoding LIF comprises the quantification of the messenger RNA (mRNA) of said gene, a fragment of said mRNA, complementary DNA (cDNA) of said gene, a fragment of

said cDNA, or mixtures thereof.

8. The method according to claim 7, wherein the quantification of the expression levels of the gene encoding LIF is performed by means of a quantitative polymerase chain reaction (PCR).

9. The method according to claim 4, wherein the quantification of the levels of protein is performed by means of Western blot, immunohistochemistry, ELISA or by means of the determination of the activity of said protein.

10. An *in vitro* method for the prognosis of life expectancy of subjects suffering from cancer, comprising quantification of the expression levels of the gene encoding LIF or of the protein encoded by said gene in a biological sample from said subject according to claim 7 to 9, wherein an increase of the expression of the gene encoding LIF or of the protein encoded by said gene, with respect to the expression of the gene encoding LIF or of the protein encoded by said gene in a control sample, is indicative of a reduced life expectancy.

11. A kit comprising reagents for the quantification of the expression levels of the gene encoding LIF or of the protein encoded by said gene for the diagnosis of cancer in a subject or for determining the predisposition of a subject to suffer from said cancer, or for determining the stage or severity of said cancer in a subject, or for monitoring the effect of the therapy administered to a subject with said cancer, wherein if the reagents detect an increase in the expression of said gene or said protein with respect to a control sample, then said subject can suffer from cancer, or present a greater predisposition to suffer from said cancer, or present a greater severity of said cancer, or the administered therapy is not being effective.

12. The use according to claim 1 or the method according to claim 5 or 6, wherein said agent or antibody acts through the inhibition of the self-regeneration of

tumor stem cells.

13. The method according to any of claims 5, 6 or 12, wherein the inhibitory agent is selected from the group consisting of siRNAs, antisense oligonucleotides, specific ribozymes, antibodies, polypeptides and inhibitors of cytokine receptor binding.

14. The method according to claim 13, wherein the antibodies are inhibitory antibodies specific to LIF or antibodies blocking the LIF receptors.

15. The use according to claim 1, the method according to any one of claims 4 to 6 or 12 to 14, or the kit according to claim 11, wherein said cancer is caused by a high activity of the JAK-STAT signaling pathway.

16. The use according to any one of claims 1, 12 or 15, the method according to any of claims 4 to 7 or 12 to 14, wherein said cancer is one of the following: glioma, pre-B cell acute lymphoblastic leukemia, acute myeloid leukemia, colorectal carcinoma, bladder cancer, breast ductal cancer or breast carcinoma.

17. The use or the method according to claim 16, wherein said glioma is grade IV glioma.

18. The use according to any one of claims 1, 12 or 15 to 17 or the method according to claim 10, wherein said cancer is characterized by presenting abnormally high levels of LIF in a subset of patients, and/or wherein the cancer tumor forming cells are characterized by presenting a concentration of LIF which is at least 5% greater than those occurring in a control sample.

19. A pharmaceutical composition comprising a therapeutically effective amount of an antibody referred to in any of claims 1, 12 or 15 to 18 together with a pharmaceutically acceptable carrier.

20. Use of the kit according to any one of claims 11 or 15.

Claims

1. Use of an inhibitory anti-LIF antibody in the manufacture of a medicament for the treatment of cancer, wherein said cancer is glioma.

2. An *in vitro* method for the identification of compounds capable of blocking/inhibiting the cell proliferation of tumor cells induced by LIF, comprising the steps of:
   (i) contacting a cell expressing the receptor for LIF with LIF and a candidate compound, and
   (ii) identifying those compounds blocking the cell proliferation of said cell,
   wherein the cell expressing the receptor for LIF is a glioma initiating cell (GIC).

3. An *in vitro* method for designing a customized therapy for a patient suffering from cancer, or for selecting patients suffering from cancer, or for the prognosis of life expectancy of subjects suffering from cancer, comprising quantifying the expression levels of the gene encoding LIF or of the protein encoded by said gene in a biological sample from said subject, wherein an increase of the expression of the gene encoding LIF or of the protein encoded by said gene, with respect to the expression of the gene encoding LIF or of the protein encoded by said gene in a control sample, is indicative of a reduced life expectancy, wherein the patient is selected to receive treatment with an inhibitory agent of LIF, and wherein the cancer is glioma.

4. An *in vitro* method for designing a customized therapy for a patient suffering from cancer according to claim 3 comprising:
   (a) quantifying the expression levels of LIF in said patient, and
   (b) comparing said expression levels with control levels,

wherein if the expression levels of LIF in said patient are greater than the control values, then an inhibitory agent of LIF is administered to said patient, wherein the inhibitory agent is an inhibitory antibody specific to LIF or an antibody blocking the LIF receptors.

5. An *in vitro* method for selecting patients suffering from cancer according to claim 3, to be treated with an inhibitory agent of LIF comprising
   (a) quantifying the expression levels of LIF in said patient, and
   (b) comparing said expression levels with control levels,
   wherein if the expression levels of LIF in said patient are greater than the control values, then said patient is selected to receive treatment with an inhibitory agent of LIF, wherein the inhibitory agent is an inhibitory antibody specific to LIF or an antibody blocking the LIF receptors.

6. The method according to claim 3, wherein the quantification of the expression levels of the gene encoding LIF comprises the quantification of the messenger RNA (mRNA) of said gene, a fragment of said mRNA, complementary DNA (cDNA) of said gene, a fragment of said cDNA, or mixtures thereof.

7. The method according to claim 4, wherein the quantification of the expression levels of the gene encoding LIF is performed by means of a quantitative polymerase chain reaction (PCR).

8. The method according to claim 3, wherein the quantification of the levels of protein is performed by means of Western blot, immunohistochemistry, ELISA or by means of the determination of the activity of said protein.

9. The use according to claim 1, or the method according to any one of claims 3 to 8, wherein said glioma is grade IV glioma.

10. The use according to claims 1 or 9, or the method according to claim 3, wherein the cancer tumor forming cells are characterized by presenting a concentration of LIF which is at least 5% greater than those occurring in a control sample.

11. A pharmaceutical composition comprising a therapeutically effective amount of an antibody referred to in any of claims 1, or 7 to 9 together with a pharmaceutically acceptable carrier.