

CLAIMS

1. An *in vitro* method for the prognosis of the survival time of a patient suffering from a solid cancer, which method comprises the following steps:

a) detecting and quantifying two or more biological markers indicative of the status of the immune response of said patient against said cancer, wherein each biological marker indicative of the status of the immune response is detected *in vitro* and quantified in a tumor sample obtained from said patient;

b) comparing each values obtained at step a) for said two or more biological markers with a distribution of values obtained for each of said two or more biological markers from a reference group of patients suffering from said cancer;

c) determining for each values obtained at step a) for said two or more biological markers the percentile of the distribution to which the values obtained at step a) correspond;

d) calculating the arithmetic mean value or the median value of percentiles of the biological markers determined in step c); and

e) comparing the arithmetic mean value or the median value of percentiles obtained at step d) with a predetermined reference arithmetic mean value or a predetermined median value of percentiles, which predetermined reference value is correlated with survival time.

2. An *in vitro* method for assessing the responsiveness of a patient suffering from a solid cancer to an antitumoral treatment, which method comprises the following steps:

a) detecting and quantifying two or more biological markers indicative of the status of the immune response of said patient against said cancer, wherein each biological marker indicative of the status of the immune response is detected *in vitro* and quantified in a tumor sample obtained from said patient;

b) comparing each values obtained at step a) for said two or more biological markers with a distribution of values obtained for each of said two or more biological markers from a reference group of patients suffering from said cancer;

c) determining for each values obtained at step a) for said two or more biological markers the percentile of the distribution to which the values obtained at step a) correspond;

d) calculating the arithmetic mean value or the median value of percentiles of the biological markers determined in step c); and

e) comparing the arithmetic mean value or the median value of percentiles obtained at step d) with a predetermined reference arithmetic mean value or a predetermined median

value of percentiles, which predetermined reference value is correlated with response to said antitumoral treatment.

3. The method according to claim 1 or 2, wherein the solid cancer is a colorectal cancer, a breast cancer, a lung cancer, a head and neck cancer, bladder cancer, a ovary cancer, or a prostate cancer.

4. The method according to claim 3, wherein the solid cancer is a colorectal cancer.

5. The method according to any of claims 1 to 4, wherein the two or more biological markers comprise the cell density of cells from the immune system.

6. The method according to claim 5, wherein the two or more biological markers comprise the density of CD3⁺ cells, the density of CD8⁺ cells, the density of CD45RO⁺ cells, the density of GZM-B⁺ cells, the density of B cells, and/or the density of DC cells.

7. The method according to claim 6, wherein the two or more biological markers comprise the density of CD3⁺ cells and the density of CD8⁺ cells, the density of CD3⁺ cells and the density of CD45RO⁺ cells, the density of CD3⁺ cells the density of GZM-B⁺ cells, the density of CD8⁺ cells and the density of CD45RO⁺ cells, the density of CD8⁺ cells and the density of GZM-B⁺ cells; or the density of CD45RO⁺ cells and the density of GZM-B⁺ cells.

8. The method according to any of claims 5 to 7, wherein the density of cells from the immune system are quantified in the center of the tumor and/or in the invasive margin of the tumor.

9. The method according to claim 8, wherein the two or more biological markers comprise the density of CD3⁺ cells in center of the tumor, the density of CD8⁺ cells in the center of the tumor, the density of CD3⁺ cells in the invasive margin, and the density of CD8⁺ cells in the invasive margin

10. The method according to any of claims 1 to 9, wherein the two or more biological markers comprise the expression level of one or more genes from the group consisting of CCR2,

CD3D, CD3E, CD3G, CD8A, CXCL10, CXCL11, GZMA, GZMB, GZMK, GZMM, IL15, IRF1, PRF1, STAT1, CD69, ICOS, CXCR3, STAT4, CCL2, and TBX21.

11. The method according to any of claims 1 to 10, wherein the two or more biological markers comprise the expression level of one or more genes from the group consisting of GZMH, IFNG, CXCL13, GNLY, LAG3, ITGAE, CCL5, CXCL9, PF4, IL17A, TSLP, REN, IHH, PROM1 and VEGFA.

12. The method according to any of claims 1 to 10, wherein the two or more biological markers comprise an expression level of at least one gene representative of human adaptive immune response and an expression level of at least one gene representative of human immunosuppressive response.

13. The method according to claim 12, wherein the at least one gene representative of human adaptive immune response is selected from the group consisting of

CCL5
CCR2
CD247
CD3E
CD3G
CD8A
CX3CL1
CXCL11
GZMA
GZMB
GZMH
GZMK
IFNG
IL15
IRF1
ITGAE
PRF1
STAT1
TBX21

and said at least one gene representative of human immunosuppressive response is selected from the group consisting of:

CD274

CTLA4
IHH
IL17A
PDCD1
PF4
PROM1
REN
TIM-3
TSLP
VEGF

14. The method according to any one of the preceding claims, wherein each biological marker is a nucleic acid.
15. The method according to any one of the preceding claims, wherein each biological marker is detected by mRNA hybridization and/or amplification.
16. The method according to any one of claims 1 to 13, wherein each biological marker is a protein.
17. The method according to any one of claims 1 to 13 and 16, wherein each biological marker is detected by immunohistochemistry.