

of CXCL5, EFNA5, EMCN, G6PC, GFPT2, HIST2H3C, IGFBP1, LAMB3, MMP9, MOCOS, PLG, PRAME, RARRES1, SDPR, SLC6A19, TK1, KDELR3 and TSPAN7 and any combinations thereof.

[0009] A kit comprising: at least one reagent to determine the level of expression for each marker of a panel of markers in a tissue tumour sample, wherein the panel comprises at least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and at least one prognostic gene selected from the group consisting of CXCL5, EFNA5, EMCN, G6PC, GFPT2, HIST2H3C, IGFBP1, LAMB3, MMP9, MOCOS, PLG, PRAME, RARRES1, SDPR, SLC6A19, TK1, KDELR3 and TSPAN7 and any combinations thereof.

[0009a] In another aspect, there is provided a method of making a prognosis as to whether a patient having renal cancer is likely to survive in a tumour tissue sample obtained from the patient comprising:

- a) determining the level of expression for each marker of a panel of markers, wherein the panel comprises at least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and prognostic genes CXCL5, EFNA5, EMCN, LAMB3, PLG, PRAME, RARRES1 and SLC6A19;
- b) determining whether an expression parameter for each marker in the tumour tissue sample is achieved by comparing the level of expression of each marker with a predetermined reference level associated with each marker;
- c) determining the differential expression of each marker in the tumour tissue sample based on the expression parameter for each marker to provide a prognosis for renal cancer;

wherein the renal cancer is clear cell renal cell carcinoma (ccRCC) or a mixed renal tumour comprising a ccRCC component.

[0009b] In another aspect, there is provided a method for
5 predicting responsiveness to an anti-renal cancer treatment in a patient having or at risk of developing renal cancer in a tumour tissue sample obtained from the patient comprising:

a) determining the level of expression for each marker of a panel of markers, wherein the panel comprises at least
10 one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and the prognostic genes CXCL5, EFNA5, EMCN, LAMB3, PLG, PRAME, RARRES1 and SLC6A19;

b) determining whether an expression parameter for each
15 marker in the tumour tissue sample is achieved by comparing the level of expression of each marker with a predetermined reference level associated with each marker;
wherein differential expression of each marker in the tumour tissue sample based on the expression parameter for each
20 marker is indicative of the responsiveness of the patient to the anti-renal cancer treatment; and
wherein the renal cancer is a clear cell renal cell carcinoma (ccRCC) or a mixed renal tumour comprising a ccRCC component.

[0009c] In another aspect, there is provided a kit comprising:
25 at least one reagent to determine the level of expression for each marker of a panel of markers in a tissue tumour sample, wherein the panel comprises at least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and prognostic genes
30 CXCL5, EFNA5, EMCN, LAMB3, PLG, PRAME, RARRES1 and SLC6A19.

DEFINITIONS

[0010] The terms "biological material" or "biological sample" as used herein refers to any material or sample, which includes an analyte as defined herein. Such samples may, for
5 example, include samples derived from or comprising stool, whole blood, serum, plasma, tears, saliva, nasal fluid, sputum, ear fluid, genital fluid, breast fluid, milk, colostrum, placental fluid, amniotic fluid, perspirate, synovial fluid, ascites fluid, cerebrospinal fluid, bile,
10 gastric fluid, aqueous humor, vitreous humor, gastrointestinal fluid, exudate, transudate, pleural fluid, pericardial fluid, semen, upper airway fluid, peritoneal fluid, fluid harvested from a site of an immune response, fluid harvested from a pooled collection site, bronchial lavage, urine, biopsy
15 material, e.g. from all suitable organs, e.g. the lung, the muscle, brain, liver, skin, pancreas, stomach, etc., a nucleated cell sample, a fluid associated with a mucosal surface, hair, or skin.

Claims

1. A method of making a prognosis as to whether a patient having renal cancer is likely to survive in a tumour tissue sample obtained from the patient comprising:
 - a) determining the level of expression for each marker of a panel of markers, wherein the panel comprises at least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and prognostic genes CXCL5, EFNA5, EMCN, LAMB3, PLG, PRAME, RARRES1 and SLC6A19;
 - b) determining whether an expression parameter for each marker in the tumour tissue sample is achieved by comparing the level of expression of each marker with a predetermined reference level associated with each marker;
 - c) determining the differential expression of each marker in the tumour tissue sample based on the expression parameter for each marker to provide a prognosis for renal cancer;
wherein the renal cancer is clear cell renal cell carcinoma (ccRCC) or a mixed renal tumour comprising a ccRCC component.
2. The method according to claim 1, wherein the prognostic genes in a) further comprise MMP9, IGFBP1, G6PC, GFPT2, HIST2H3C, MOCOS, SDPR, TK1, KDELR3, TSPAN7 or any combinations thereof.
3. The method according to claim 2, wherein the further prognostic genes are MMP9 and IGFBP1.

4. The method according to claim 3, wherein the patient suffers from ccRCC or wherein the patient suffers from ccRCC and undergoes anti-cancer treatment.
5. The method according to claims 1-4, wherein said likelihood of survival correlates with a decrease in the likelihood of metastasis, disease recurrence or early death.
- 10 6. The method according to claim 1, wherein the tumour tissue sample is obtained from tissue selected from the group consisting of frozen tissue, tissue biopsies, circulating tumour cells and bodily fluids.
- 15 7. The method according to claim 6, wherein the bodily fluids are selected from the group consisting of ascites, effusions, cerebrospinal and urine.
8. The method according to claim 1, wherein the patient is
20 undergoing anti-cancer treatment.
9. The method according to claim 8, wherein the anti-cancer treatment is selected from the group consisting of a chemotherapeutic treatment, a surgical treatment, a
25 treatment with radiation therapy, immunotherapy, targeted therapy, small molecule therapeutics or any combination thereof.
10. The method according to claim 9, wherein the
30 chemotherapeutic treatment comprises treatment with a protein kinase inhibitor, receptor tyrosine kinase inhibitor, antimetabolite, platinum complex, spindle poison,

DNA crosslinking drug and alkylating agent, bleomycin, antibiotic, and topoisomerase inhibitor or combinations thereof.

- 5 11. The method according to claim 10, wherein the receptor tyrosine kinase inhibitor is selected from the group consisting of sunitinib, pazopanib, axitinib, sorafenib or combinations thereof.
- 10 12. The method according to claim 10, wherein the protein kinase inhibitor is temsirolimus or everolimus.
13. The method according to claim 9, wherein the targeted therapy comprises anti-tumour antibodies such as
15 bevacizumab, interferon and combinations thereof.
14. The method according to claim 9, wherein the immunotherapy is interferon, high-dose-interleukin 2 or combinations thereof.
- 20 15. The method according to claim 9, wherein the small molecule therapeutics comprises tivozanib.
16. The method according to claim 1, wherein the patient is a
25 mammal or a human.
17. The method according claim 16, wherein the human is an ethnic Asian, or an ethnic Caucasian, or an ethnic African.
- 30 18. The method of claim 1, wherein the predetermined reference level is determined based on the expression of the at least one housekeeping gene.

19. The method of claim 1, wherein the determining of whether or not the biomarkers are differentially expressed in the sample further comprises normalizing the levels of expression of the markers to the at least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof.
20. The method of claim 19, wherein the levels of expression of the markers are normalized against the geometric mean C_T value of the at least one housekeeping gene.
21. The method according to claim 2, wherein an increase in the expression parameter of prognostic genes selected from the group consisting of EMCN, G6PC, PLG, SDPR, SLC6A19 and TSPAN7 indicates an increased chance of survival.
22. The method according to claim 2, wherein a decrease or absence in the expression parameter of prognostic genes selected from the group consisting of G6PC, PLG, SDPR, SLC6A19 and TSPAN7 indicates a decreased chance of survival.
23. The method according to claim 2, wherein an increase in the expression parameter of prognostic genes CXCL5, EFNA5, GFPT2, HIST2H3C, IGFBP1, LAMB3, MMP9, MOCOS, PRAME, RARRES1 and TK1 indicates a decreased chance of survival.
24. The method according to claim 2, wherein a decrease or absence in the expression parameter of prognostic genes GFPT2 and LAMB3 indicates an increased chance of survival.
25. The method according to any one of the preceding claims, wherein the prognosis is determined by a multivariate algorithm.

26. The method according to claim 25, wherein the multivariate algorithm uses a class prediction approach.
- 5 27. The method according to claim 26, wherein the class prediction approach used is prediction analysis for microarrays (PAMR).
- 10 28. The method according to any of claims 25 to 27 wherein the multivariate algorithm is multivariate logistic correlation analysis, wherein the multivariate logistic correlation analysis is used to score the prognostic genes CXCL5, LAMB3, MMP9, PRAME, RARRES1, PLG, SLC6A19, EFNA5, IGFBP1 and EMCN.
- 15 29. The method of claim 28, wherein the multivariate logistic correlation analysis is calculated using the scoring formula:
- 0.00534xCXCL5 -0.0111xLAMB3 +0.001578xMMP9 -0.02952xPRAME
 -0.01001xRARRES1 +0.012535xPLG +0.021832xSLC6A19 -
 20 0.01494xEFNA5 +0.014457xIGFBP1 +0.020579xEMCN
30. A method for predicting responsiveness to an anti-renal cancer treatment in a patient having or at risk of
 25 developing renal cancer in a tumour tissue sample obtained from the patient comprising:
- a) determining the level of expression for each marker of a panel of markers, wherein the panel comprises at
 30 least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and the prognostic genes CXCL5, EFNA5, EMCN, LAMB3, PLG, PRAME, RARRES1 and SLC6A19;

b) determining whether an expression parameter for each marker in the tumour tissue sample is achieved by comparing the level of expression of each marker with a predetermined reference level associated with each marker; wherein differential expression of each marker in the tumour tissue sample based on the expression parameter for each marker is indicative of the responsiveness of the patient to the anti-renal cancer treatment; and wherein the renal cancer is a clear cell renal cell carcinoma (ccRCC) or a mixed renal tumour comprising a ccRCC component.

31. The method according to claim 30, wherein the prognostic genes in a) further comprise MMP9, IGFBP1, G6PC, GFPT2, HIST2H3C, MOCOS, SDPR, TK1, KDELR3, TSPAN7 or any combinations thereof.

32. The method according to claim 31, wherein the further prognostic genes are MMP9 and IGFBP1.

33. The method according to any of claims 30 to 32, wherein an increase in the expression parameter of prognostic genes EMCN, G6PC, PLG, SDPR, SLC6A19 and TSPAN7 indicates an increased responsiveness to the treatment and an increased chance of survival.

34. The method according to claim 30, wherein a decrease or absence in the expression parameter of prognostic genes EMCN, G6PC, PLG, SDPR, SLC6A19 and TSPAN7 indicates a decreased responsiveness to the treatment and a decreased chance of survival.

35. The method according to claim 30, wherein an increase in the expression parameter of prognostic genes CXCL5, EFNA5,

GFPT2, HIST2H3C, IGFBP1, LAMB3, MMP9, MOCOS, PRAME, RARRES1 and TK1 indicates a decreased responsiveness to the treatment and a decreased chance of survival.

5 36. The method according to claim 30, wherein a decrease or absence in the expression parameter of prognostic genes CXCL5, EFNA5, GFPT2, HIST2H3C, IGFBP1, LAMB3, MMP9, MOCOS, PRAME, RARRES1 and TK1 indicates an increased responsiveness to the treatment and an increased chance of survival.

10 37. The method according to any one of claims 1 to 36, wherein determining the level of expression of each marker comprises:

15 a. contacting a nucleic acid sequence obtained or derived from said sample with at least one primer and/or at least one probe for amplification of a sequence of the marker;

b. amplifying said nucleic acid sequence using said at least one primer or probe with a polymerase enzyme;

20 c. detecting the level of expression of the marker in said sample.

38. The method according to claim 37, wherein said amplification step is performed by polymerase chain reaction (PCR).

25 39. A kit comprising:

at least one reagent to determine the level of expression for each marker of a panel of markers in a tissue tumour sample, wherein the panel comprises at least one housekeeping gene selected from the group consisting of ACTB, RPL13A, RPL9, and RPS29 and any combinations thereof; and prognostic genes CXCL5, EFNA5, EMCN, LAMB3, PLG, PRAME, RARRES1 and SLC6A19.

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40. The kit according to claim 39, wherein the prognostic gene in a) further comprise MMP9, IGFBP1, G6PC, GFPT2, HIST2H3C, MOCOS, SDPR, TK1, KDEL3, TSPAN7 or any combinations thereof.

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41. The kit according to claim 39, wherein the further prognostic genes are MMP9 and IGFBP1.

10 42. The kit according to any of claims 39 to 41, wherein the at least one reagent comprises:
at least one primer and/or at least one probe for amplification of a sequence comprising the marker.