

using primary CC-RCC specimens, metastatic specimens and non-cancerous unmatched cortical specimens has identified nucleic acid sequences (WO 2006/124022). Y. Masahiro, et al., (Int J Cancer 123:5 (2008)), developed a three-gene expression signature model to predict clinical outcome of CC-RCC, and showed that VCAM1, EDNRB and RGS5 were associated with cancer-specific survival and that higher expression correlated with better outcome.

SUMMARY

[0006] The present disclosure provides biomarkers, the expression of which has prognostic value in renal cancer.

In one aspect, the present disclosure provides a method comprising: (a) measuring, in a biological sample obtained from a cancer patient with renal cell carcinoma, an expression level of an RNA transcript of PPAP2B, or its expression product; (b) normalizing the expression level to obtain a normalized expression level; and (c) determining a likelihood of recurrence of renal cell carcinoma for the patient by comparing the normalized expression level of PPAP2B to gene expression data obtained from a renal cell carcinoma sample from a population of patients with known clinical outcome with respect to recurrence of renal cell carcinoma, wherein increased normalized expression level of PPAP2B is negatively correlated with a risk of a recurrence of renal cell carcinoma.

In another aspect, the present disclosure provides a method comprising: (a) measuring, in a biological sample obtained from a cancer patient with renal cell carcinoma, an expression level of an RNA transcript of PPAP2B, or its expression product; (b) normalizing the expression level to obtain a normalized expression level; and (c) determining a likelihood of an increased tumour stage for the patient by comparing the normalized expression level of PPAP2B to gene expression data obtained from a renal cell carcinoma sample from a population of patients with known clinical outcome with respect to stage of the tumour, wherein increased normalized expression level of PPAP2B is negatively correlated with increased stage of the tumour.

In another aspect, the present disclosure provides a method comprising: (a) measuring, in a biological sample obtained from a cancer patient with renal cell carcinoma, an expression level of an RNA transcript of PPAP2B, or its expression product; (b) normalizing

the expression level to obtain a normalized expression level; and (c) determining a likelihood of an increased tumour grade for the patient by comparing the normalized expression level of PPAP2B to gene expression data obtained from a renal carcinoma sample from a population of patients with known clinical outcome with respect to grade of the tumour, wherein increased normalized expression level of PPAP2B is negatively correlated with increased grade of the tumour.

In another aspect, the present disclosure provides a method comprising: (a) measuring, in a biological sample obtained from a cancer patient with renal cell carcinoma, an expression level of an RNA transcript of PPAP2B, or its expression product; (b) normalizing the expression level to obtain a normalized expression level; and (c) determining the presence of necrosis for the patient by comparing the normalized expression level of PPAP2B to gene expression data obtained from a renal carcinoma sample from a population of patients with known clinical outcome with respect to presence of necrosis, wherein increased normalized expression level of PPAP2B is negatively correlated with the presence of necrosis.

In another aspect, the present disclosure provides a method comprising: (a) measuring, in a biological sample obtained from a cancer patient with renal cell carcinoma, an expression level of an RNA transcript of PPAP2B, or its expression product; (b) normalizing the expression level to obtain a normalized expression level; and (c) determining a nodal status of the patient by comparing the normalized expression level of PPAP2B to gene expression data obtained from a renal carcinoma sample from a population of patients with known clinical outcome with respect to nodal invasion, wherein increased normalized expression level of PPAP2B is negatively correlated with nodal invasion.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] Figures 1a-1c: Consistency between Stage I and III for exemplary genes associated with RFI

[0008] Figure 2: Consistent results across endpoints (OS and RFI) for exemplary genes

[0009] Figure 3: Kaplan-Meier curve: Recurrence Free Internal (RFI) by Cleveland Clinic Foundation (CCF) histologic necrosis

- [0010] Figure 4: Performance of Mayo prognostic tool applied to CCF data
- [0011] Figure 5: Example of using one gene to improve estimate: EMCN in addition to Mayo Criteria
- [0012] Figure 6: Example of using one gene to improve estimate: AQP1 in addition to Mayo Criteria
- [0013] Figure 7: Example of using one gene to improve estimate: PPAP2B in addition to Mayo Criteria

DETAILED DESCRIPTION

DEFINITIONS

- [0014] Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Singleton *et al.*, Dictionary of Microbiology and Molecular Biology 2nd ed., J. Wiley & Sons (New York, NY 1994), and March, Advanced Organic Chemistry Reactions, Mechanisms and Structure 4th ed., John Wiley & Sons (New York, NY 1992), provide one skilled in the art with a general guide to many of the terms used in the present application.
- [0015] One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. Indeed, the present invention is in no way limited to the methods and materials described. For purposes of the present invention, the following terms are defined below.