art adequately address early detection of bladder cancer. For example, tests that measure Nuclear Matrix Protein 22 (NMP22) and Bladder Tumour Antigen (BTA) are currently available commercially and have been approved by the U.S. Food and Drug Administration (FDA) for bladder carcinoma diagnosis. However, these tests rely on single-marker assays that are known to lack specificity.

[0007] As none of the single biomarker assays known in the art adequately address early detection of bladder cancer, there is a need to provide an alternative assay that is able to address early detection of bladder cancer. For example, two multiplex protein signatures of ten biomarkers or eight biomarkers have been developed and known in the art. However, none of these currently available diagnostic marker assays have offered sufficient sensitivity and specificity to be routinely used in the clinic.

[0008] In view of the above, there is a need to provide an alternative bladder cancer protein biomarker. There is also a need to provide an alternative detection system for non-invasive detection of bladder cancer in a patient. There is also a need to provide an alternative method of determining whether a patient suffers from or shows recurrence of bladder cancer or early stage bladder cancer or late stage bladder cancer.

SUMMARY OF THE INVENTION

[0009] In one aspect, there is provided a combination of bladder cancer protein biomarkers, wherein the biomarker are at least one selected from the group of consisting of Coronin-1A, Apolipoprotein A-IV, Semenogelin-2, Gamma-synuclein and DJ-1; wherein the variant is an allelic variant, splice variant or any other species specific homolog, paralog, or ortholog; and wherein the biomarkers are to be detected in a urine or voided urine sample.

[0010] In another aspect, there is provided a detection system comprising a) a receiving section to receive a urine or voided urine fluid sample from a patient suspected to suffer from bladder cancer and wherein the fluid sample is suspected to comprise the combination of biomarkers according to the present invention and b) a detection section comprising a substance or substances capable to detect the biomarkers according to the present invention.

[0011] In yet another aspect, there is provided a method of determining whether a patient suffers from or shows recurrence of bladder cancer or early stage bladder cancer or late stage bladder cancer, wherein the method comprises detecting the presence of the biomarkers according to the present invention in a urine or voided urine sample, wherein the indication as to whether the biomarkers are comprised in a sample obtained from the patient is made based on comparison of the results with a control group, wherein the control group comprises patients which do not suffer from bladder cancer; and wherein the level of the biomarkers is increased in the patient that suffers from or shows recurrence of bladder cancer or early stage bladder cancer or late stage bladder cancer compared to the patients which do not suffer from bladder cancer.

[0012] In yet another aspect there is provided a kit comprising a detection system according to the present invention and substances needed to carry out the method according to the present invention.

Claims

1. A combination of bladder cancer biomarkers, wherein the biomarkers are at least three selected from the group consisting of Coronin-1A, Apolipoprotein A-IV, Semenogelin-2, Gamma-synuclein and DJ-1, and variants thereof; wherein the variant is an allelic variant, splice variant or any other species specific homolog, paralog, or ortholog; and wherein the biomarkers are to be detected in a urine or voided urine sample.

2. The combination of bladder cancer biomarkers of claim 1, wherein the biomarker is indicative for early stage (Ta/T1) and/or late stage (T2/T3) bladder cancer.

3. The combination of bladder cancer biomarkers of claim 1 or 2, wherein the biomarkers are Coronin-1A, Apolipoprotein A-IV, Semenogelin-2, Gamma-synuclein and DJ-1.

4. A detection system comprising a) a receiving section to receive a urine or voided urine sample from a patient suspected to suffer from bladder cancer and wherein the sample is suspected to comprise the combination of biomarkers as defined in any one of claims 1 to 3 and b) a detection section comprising a substance or substances capable of detecting the biomarkers as defined in any one of claims 1 to 3.

5. The detection system of claim 4, wherein the detection section comprises a substance capable of binding or specifically binding to the biomarkers as defined in any one of claims 1 to 3.

6. The detection system of claim 5, wherein the substance is a biospecific capture reagent selected from the group consisting of antibodies or antigen-binding fragment thereof, interacting fusion proteins, aptamers and affibodies.

7. The detection system of any of claims 4 to 6, wherein the system is a biochip or test strip or microtiter plate.

8. A method of determining whether a patient suffers from or shows recurrence of bladder cancer or early stage bladder cancer or late stage bladder cancer, wherein the method comprises detecting the presence of the biomarkers as defined in any one of claims 1 to 3 in a urine or voided urine sample, wherein the indication as to whether the biomarkers are comprised in a sample obtained from the patient is made based on comparison of the results with a control group, wherein the control group comprises patients which do not suffer from bladder cancer; and wherein the level of the biomarkers is increased in the patient that suffers from or shows recurrence of bladder cancer or early stage bladder cancer or late stage bladder cancer compared to the patients which do not suffer from bladder cancer.

9. The method of claim 8, wherein detection is carried out using molecular biological methods.

10. The method of claim 9, wherein the molecular biological methods are selected from the group consisting of polymerase chain reaction (PCR), Western Blot, dot blot, mass spectrometry and immunological methods.

11. The method of any one of claims 8 to 10, wherein the method measures RNA expression.

12. The method of any one of claims 8 to 10, wherein the method measures protein expression.

13. The method of any one of claims 8 to 12 wherein the method uses a detection system according to any one of claims 4 to 7.

14. A kit comprising a detection system according to any one of claims 4 to 7 and substances needed to carry out the method according to any one of claims 8 to 13.