view of the recent finding that PSA screening fails in reducing mortality, there remain significant needs for development of agents and methods that can provide reliable results in the diagnosis and prognosis of prostate cancer.

SUMMARY

[0004a] In one aspect, there is provided a method for diagnosing prostate cancer in a test subject, comprising:

a) contacting cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the cancer cells are from a blood sample that has been taken from the test subject; and

b) determining whether any of the cancer cells express the prostate-specific marker, wherein the presence of cancer cells that express the prostate-specific marker is predictive of having prostate cancer in the test subject.

[0005] In one ~~aspect~~embodiment, the present disclosure provides methods for diagnosing prostate cancer in a test subject, comprising: a) contacting cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the cancer cells are from a blood sample taken from the test subject; and b) determining whether any of the cancer cells express the prostate-specific marker, wherein the presence of cancer cells that express the prostate-specific marker is predictive of having prostate cancer in the test subject.

[0006] In certain embodiments, the method further comprises determining the amount of the cancer cells that express the prostate-specific marker, wherein such amount is predictive of the stage of prostate cancer in the test subject.

[0007] In certain embodiments, the method further comprises determining the expression level of the prostate-specific marker on the cancer cells.

[0008] In certain embodiments, the method further comprises grading the cancer cells based on their expression level of the prostate-specific marker, and determining the percentage of the cancer cells in each grade.

[0009] In certain embodiments, the method further comprises calculating a grade score for each grade by multiplying the percentage of the cancer cells in that grade with a unique grade number assigned to that grade based on the expression level of the prostate-specific marker, and summing up all the grade scores to obtain an H score, wherein the H score is indicative of the stage of the prostate cancer in the test subject.

[0010] In certain embodiments, the cancer cells are identified from the blood sample with a capturing composition comprising a ligand that specifically binds to cancer cells of epithelial origin. In certain embodiments, the ligand is an antibody that specifically binds to an epithelial antigen preferentially

expressed on cancer cells. In certain embodiments, the epithelial antigen is Epithelial Cell Adhesion Molecule (EpCAM).

[0011] In certain embodiments, the identified cancer cells are enriched in a cell fraction separated from the blood sample. In certain embodiments, the cell fraction is separated under a magnetic field. In certain embodiments, the ligand in the capturing composition is coupled to a magnetic particle.

[0012] In certain embodiments, the antibody that specifically binds to a prostate-specific marker comprises an anti-STEAP-1 antibody. In certain embodiments, the anti-STEAP-1 antibody binds to STEAP-1 with a KD of $\leq$ 1000 nM. In certain embodiments, the anti-STEAP-1 antibody is a murine

monoclonal antibody. In certain embodiments, the anti-STEAP-1 antibody is 15A5, produced by a hybridoma cell having a microorganism deposit number PTA-12259.

[0013] In certain embodiments, the cancer cells are identified with one or more reagents that allow detection of cancer cells of epithelial origin. In certain embodiments, the reagents comprise a ligand that specifically binds to a cytokeratin, and wherein the ligand is optionally conjugated with a second detectable label. In certain embodiments, the reagents further comprise a dye that differentiates cells from non-cell components. In certain embodiments, the reagents further comprise a ligand that specifically binds to a leukocyte marker.

[0014] In certain embodiments, the cancer cells are detected by a method based on immunofluorescent microscopy, flow cytometry, fiber-optic scanning cytometry, or laser scanning cytometry.

[0014a] In one aspect, there is provided a method of predicting efficacy of prostate cancer therapy in a test subject, comprising:

a) contacting cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the cancer cells are from a blood sample that has been taken from the test subject; and

b) determining whether any of the cancer cells express the prostate-specific marker, wherein the presence of cancer cells that express the prostate-specific marker is predictive of the efficacy of the prostate cancer therapy in the test subject.

[0015] In another ~~aspect~~embodiment, the present disclosure provides methods of predicting efficacy of prostate cancer therapy in a test subject.

[0015a] In one aspect, there is provided a method of monitoring response to a prostate cancer therapy in a test subject, comprising:

a) contacting a first group of cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the first group of cancer cells are from a first blood sample that has been taken from the test subject;

b) determining the amount of the cancer cells in the first group that express prostate-specific marker and/or the expression level of the prostate-specific marker in the cancer cells;

c) contacting a second group of cancer cells of epithelial origin with the antibody that specifically binds to a prostate-specific marker, wherein the second group of cancer cells are from a second blood sample that has been taken from the test subject after a test period of prostate cancer therapy;

d) determining the amount of the cancer cells in the second group that express prostate-specific marker and/or the expression level of the prostate-specific marker in the cancer cells; and

e) comparing the amount of the cancer cells that express the prostate-specific marker and/or the prostate-specific marker expression level as determined in b) with that in d),

wherein a decrease in the amount of the cancer cells expressing the prostate-specific marker and/or a decrease in the prostate-specific marker expression level in the cancer cells indicates a response to the prostate cancer therapy in the test subject.

[0016] In another ~~aspect~~embodiment, the present disclosure provides methods of monitoring response to a prostate cancer therapy in a test subject.

[0016a] In one aspect, there is provided an antibody which binds to substantially the same epitope to which antibody 15A5 binds, wherein antibody 15A5 is produced by a hybridoma cell having a microorganism deposit number of: PTA-12259.

[0017] In another ~~aspect~~embodiment, the present disclosure provides antibodies which binds to substantially the same epitope to which antibody 15A5 binds, wherein antibody 15A5 is produced by a hybridoma cell having a microorganism deposit number of PTA-12259.

[0017a] In one aspect, there is provided an isolated polynucleotide encoding the antibody as defined herein.

[0017b] In one aspect, there is provided a host cell comprising the polynucleotide as defined herein.

[0017c] In one aspect, there is provided a hybridoma cell line having a microorganism deposit number of PTA-12259.

[0018] In another ~~aspect~~embodiment, the present disclosure provides a hybridoma cell line having a microorganism deposit number of PTA-12259.

[0018a] In another aspect, there is provided a test kit for detecting presence of prostate cancer cells expressing STEAP-1 in a blood sample, comprising an antibody that specifically binds to STEAP-1.

[0019] In another ~~aspect~~embodiment, the present disclosure provides test kits for detecting presence of prostate cancer cells expressing STEAP-1 in a blood sample, comprising an antibody that specifically binds to STEAP-1. In certain embodiments, the test kits further comprises one or more compositions selected from the group consisting of: magnetic particles coupled to a first ligand that specifically binds to cancer cells of epithelial origin, a second ligand that specifically binds to an epithelial marker, a third ligand that specifically binds to a leukocyte marker, and a dye that differentiates cells from non-cell components.

[0019a] In one aspect, there is provided a use of the antibody as defined herein or an antigen-binding fragment thereof in the manufacture of a diagnostic agent for prostate cancer.

BRIEF DESCRIPTION OF THE FIGURES

[0020] **Figure 1** depicts the representative scoring criteria for CTCs based on the level of staining by an anti-STEAP-1 antibody.

[0021] **Figure 2** depicts the STEAP-1 expression and H scores of different cell lines as determined on CellSearch® system using a sheep polyclonal anti-STEAP-1 antibody, a mouse monoclonal anti-STEAP-1antibody 37, and a rabbit polyclonal anti-STEAP-1 antibody: (a) expression on LB50 cells; (b) expression on PC3 cells; (c) H score of LB50 cells; and (d) H score of PC3 cells.

WHAT IS CLAIMED IS:

1. A method for diagnosing prostate cancer in a test subject, comprising:

a) contacting cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the cancer cells are from a blood sample that has been taken from the test subject; and

b) determining whether any of the cancer cells express the prostate-specific marker, wherein the presence of cancer cells that express the prostate-specific marker is predictive of having prostate cancer in the test subject.

2. The method of claim 1, further comprising determining the amount of the cancer cells that express the prostate-specific marker, wherein such amount is predictive of the stage of prostate cancer in the test subject.
3. The method of any one of claims 1-2, further comprising determining the expression level of the prostate-specific marker on the cancer cells.
4. The method of any one of claims 1-3, further comprising grading the cancer cells based on their expression level of the prostate-specific marker, and determining the percentage of the cancer cells in each grade.
5. The method of any one of claims 1-4, further comprising calculating a grade score for each grade by multiplying the percentage of the cancer cells in said grade with a unique grade number representative of the expression level of the prostate-specific marker in said grade, and summing up all the grade scores to obtain an H score, wherein the H score is indicative of the stage of the prostate cancer in the test subject.
6. The method of any one of claims 1-5, wherein the cancer cells are identified from the blood sample with a capturing composition comprising a ligand that specifically binds to cancer cells of epithelial origin.
7. The method of claim 6, wherein the ligand is an antibody that specifically binds to an epithelial antigen preferentially expressed on cancer cells.
8. The method of claim 7, wherein the epithelial antigen is Epithelial Cell Adhesion Molecule (EpCAM).
9. The method of any one of claims 6-8, wherein the identified cancer cells are enriched in a cell fraction separated from the blood sample.
10. The method of claim 9, wherein the cell fraction is separated under a magnetic field.
11. The method of claim 10, wherein the ligand in the capturing composition is coupled to a magnetic particle (*e.g.*, colloidal magnetic particle, *e.g.*, colloidal magnetic nanoparticles). .
12. The method of claim 11, wherein the ligand comprises an EpCAM antibody.
13. The method of any of claims 1-12, wherein the prostate-specific marker is selected from the group consisting of: a Six-Transmembrane Epithelial Antigen of the Prostate (STEAP), Prostate-

specific membrane antigen (PSMA), Prostate carcinoma tumor antigen (PCTA-1), and Prostate stem cell antigen (PSCA).

14. The method of any of claims 1-13, wherein the antibody that specifically binds to a prostate-specific marker comprises an anti-STEAP-1 antibody.
15. The method of claim 14, wherein the anti-STEAP-1 antibody binds to STEAP-1 with a K_D of $\leq$ 1000 nM.
16. The method of any one of claims 14-15, wherein the anti-STEAP-1 antibody is a polyclonal antibody or a monoclonal antibody.
17. The method of claim 16, wherein the anti-STEAP-1 antibody is a murine monoclonal antibody.
18. The method of claim 17, wherein the anti-STEAP-1 antibody is 15A5, produced by a hybridoma cell having a microorganism deposit number of PTA-12259.
19. The method of any one of claims 14-18, wherein the anti-STEAP-1 antibody is conjugated with a first detectable label.
20. The method of any one of claims 1-19, wherein the cancer cells are identified with one or more reagents that allow detection of cancer cells of epithelial origin.
21. The method of claim 20, wherein the reagents comprise a ligand that specifically binds to a cytokeratin, and wherein the ligand is optionally conjugated with a second detectable label.
22. The method of any one of claims 20-21, wherein the reagents further comprise a dye that differentiates cells from non-cell components.
23. The method of claim 22, wherein the dye is 4',6-diamidino-2-phenylindole (DAPI).
24. The method of any one of claims 20-23, wherein the reagents further comprise a ligand that specifically binds to a leukocyte marker, and wherein the ligand is optionally conjugated with a third detectable label.
25. The method of claim 24, wherein the ligand to a leukocyte marker is a CD45 antibody.
26. The method of any one of claims 1-25, wherein the determining is by a method based on immunofluorescent microscopy, flow cytometry, fiber-optic scanning cytometry, or laser scanning cytometry.
27. A method of predicting efficacy of prostate cancer therapy in a test subject, comprising:

a) contacting cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the cancer cells are from a blood sample that has been taken from the test subject; and

b) determining whether any of the cancer cells express the prostate-specific marker, wherein the presence of cancer cells that express the prostate-specific marker is predictive of the efficacy of the prostate cancer therapy in the test subject.

28. A method of monitoring response to a prostate cancer therapy in a test subject, comprising:

a) contacting a first group of cancer cells of epithelial origin with an antibody that specifically binds to a prostate-specific marker, wherein the first group of cancer cells are from a first blood sample that has been taken from the test subject;

b) determining the amount of the cancer cells in the first group that express prostate-specific marker and/or the expression level of the prostate-specific marker in the cancer cells;

c) contacting a second group of cancer cells of epithelial origin with the antibody that specifically binds to a prostate-specific marker, wherein the second group of cancer cells are from a second blood sample that has been taken from the test subject after a test period of prostate cancer therapy;

d) determining the amount of the cancer cells in the second group that express prostate-specific marker and/or the expression level of the prostate-specific marker in the cancer cells; and

e) comparing the amount of the cancer cells that express the prostate-specific marker and/or the prostate-specific marker expression level as determined in b) with that in d),

wherein a decrease in the amount of the cancer cells expressing the prostate-specific marker and/or a decrease in the prostate-specific marker expression level in the cancer cells indicates a response to the prostate cancer therapy in the test subject.

29. The method of any one of claims 27-28, wherein the prostate cancer therapy comprises an antibody or antibody-drug conjugate (ADC) that binds to the prostate-specific marker.
30. The method of claim 29, wherein the prostate-specific marker is STEAP-1.
31. The method of any one of claims 27-30, wherein the ADC comprises an anti-STEAP-1 antibody covalently attached to a cytotoxic agent.
32. The method of claim 31, wherein the cytotoxic agent is selected from a toxin, a chemotherapeutic agent, a drug moiety, monomethylauristatin E (MMAE), an antibiotic, a radioactive isotope, and a nucleolytic enzyme.
33. An antibody which binds to substantially the same epitope to which antibody 15A5 binds, wherein antibody 15A5 is produced by a hybridoma cell having a microorganism deposit number of: PTA-12259.
34. The antibody of claim 33, which comprises at least one of the CDR regions of the antibody 15A5.
35. The antibody of claim 34, which comprises the six CDR regions of the antibody 15A5.
36. The antibody of any one of claims 33-35, which comprises the heavy chain variable region of the antibody 15A5.
37. The antibody of any one of claims 33-36, which comprises the light chain variable region of the antibody 15A5.
38. The antibody of any one of claims 33-37, which is antibody 15A5 or an antigen binding fragment thereof.
39. The antibody of any one of claims 33-38, further conjugated to a detectable label.