

CLAIMS

1. A human monoclonal antibody or antigen binding fragment thereof, which selectively binds prostasomes.

5

2. The human monoclonal antibody or antigen binding fragment thereof according to claim 1, wherein the human monoclonal antibody or antigen binding fragment thereof is a full-length antibody, an antigen binding (Fab) fragment, or an antigen binding single chain Fv (scFv) fragment, such as a human synthetic scFv fragment.

10

3. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-2, wherein the monoclonal antibody or antigen binding fragment thereof selectively binds prostasomes by binding one or more prostatic surface antigens, the prostatic surface antigens being selected from the group consisting of SEQ ID NO: 60-104.

15

4. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-3, wherein the monoclonal antibody or antigen binding fragment thereof selectively binds prostasomes by binding a plurality of prostatic surface antigens.

20

5. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-4, wherein the monoclonal antibody or antigen binding fragment thereof selectively binds prostasomes by binding a plurality of prostatic surface antigens, wherein the prostatic surface antigens form a conglomerate on the prostatic membrane, which conglomerate is identified and bound by the monoclonal antibody or antigen binding fragment thereof.

25

6. The human monoclonal antibody or antigen binding fragment thereof according to claim 5, wherein the conglomerate comprise at least five antigens selected from table 11.

30

7. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-6, wherein the antibody or antigen binding fragment thereof enable a sensitivity of at least 10 ng/mL in an immunoassay using the human monoclonal antibody or antigen binding fragment thereof as a capturing antibody in the immunoassay.

8. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-7, wherein the monoclonal antibody or antigen binding fragment thereof comprises a heavy chain complementary determining region (CDR) being selected from SEQ ID NO: 1-12, and a light chain CDR being selected from SEQ ID NO: 13-24.

5

9. The human antigen binding fragment according to any one of claims 1-8, wherein the antibody or antigen binding fragment thereof comprises at least six complementary determining regions (CDRs) in any combination of CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2 and CDR-L3, wherein the CDRs are selected from the group comprising:

- 10 CDR-H1 selected from SEQ ID NO: 25, 27 and 28;
- CDR-H2 selected from SEQ ID NO: 26, 29 and 30;
- CDR-H3 selected from SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12;
- CDR-L1 is selected from any variant of SEQ ID NO: 56 and 57;
- CDR-L2 is selected from any variant of SEQ ID NO: 58 and 59;
- 15 CDR-L3 selected from SEQ ID NO: 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 and 24.

10. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-9, wherein the antibody or antigen binding fragment thereof is a an antigen binding single chain Fv (scFv) fragment, such as a human synthetic scFv fragment, and wherein the scFv fragment comprises at least four complementary determining regions (CDRs) in any combination of CDR-H1, CDR-H2, CDR-H3 and CDR-L3, wherein the CDRs are selected from the group comprising:

- CDR-H1 selected from SEQ ID NO: 25, 27 and 28;
- CDR-H2 selected from SEQ ID NO: 26, 29 and 30;
- 25 CDR-H3 selected from SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12;
- CDR-L3 selected from SEQ ID NO: 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23.

11. The human monoclonal antibody or antigen binding fragment thereof according to claims 9 or 10, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NO: 32-43 and sequences having 70 % or more, such as 75 %, 80 %, 85 %, 90 %, 95 % or more, identity thereto, and a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NO: 44-55 and sequences having 70 % or more, such as 75 %, 80 %, 85 %, 90 %, 95 % or more, identity thereto.

35

12. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-11, wherein the antibody or antigen binding fragment thereof is a synthetic scFv fragment selected from the group comprising:

i) an scFv fragment having

- 5 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:4 and
CDR-L3 as defined by SEQ ID NO:16,

ii) an scFv fragment having

- 10 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:7 and
CDR-L3 as defined by SEQ ID NO:19,

iii) an scFv fragment having

- 15 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:1 and
CDR-L3 as defined by SEQ ID NO:13,

iv) an scFv fragment having

- 20 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:2 and
CDR-L3 as defined by SEQ ID NO:14,

v) an scFv fragment having

- 25 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:3 and
CDR-L3 as defined by SEQ ID NO:15,

vi) an scFv fragment having

- 30 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:5 and
CDR-L3 as defined by SEQ ID NO:17,

vii) an scFv fragment having

- 35 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:6 and

- CDR-L3 as defined by SEQ ID NO:18,
viii) an scFv fragment having
CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
5 CDR-H3 as defined by SEQ ID NO:8 and
CDR-L3 as defined by SEQ ID NO:20,
ix) an scFv fragment having
CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
10 CDR-H3 as defined by SEQ ID NO:9 and
CDR-L3 as defined by SEQ ID NO:21,
x) an scFv fragment having
CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
15 CDR-H3 as defined by SEQ ID NO:10 and
CDR-L3 as defined by SEQ ID NO:22,
xi) an scFv fragment having
CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
20 CDR-H3 as defined by SEQ ID NO:11 and
CDR-L3 as defined by SEQ ID NO:23,
xii) an scFv fragment having
CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
25 CDR-H3 as defined by SEQ ID NO:12 and
CDR-L3 as defined by SEQ ID NO:24.

13. The human monoclonal antibody or antigen binding fragment thereof according to claim 12, wherein the antibody or antigen binding fragment thereof is a synthetic scFv
30 fragment having a variable heavy chain, VH, and a variable light chain, VL, connected via a linker, wherein the fragments are selected from the group comprising:

- i) an scFv fragment having
a VH as defined by SEQ ID NO:35 and
a VL as defined by SEQ ID NO:47,
35 ii) an scFv fragment having
a VH as defined by SEQ ID NO:38 and
a VL as defined by SEQ ID NO:50,

- iii) an scFv fragment having
a VH as defined by SEQ ID NO:32 and
a VL as defined by SEQ ID NO:44,
iv) an scFv fragment having
5 a VH as defined by SEQ ID NO:33 and
a VL as defined by SEQ ID NO:45,
v) an scFv fragment having
a VH as defined by SEQ ID NO:34 and
a VL as defined by SEQ ID NO:46,
10 vi) an scFv fragment having
a VH as defined by SEQ ID NO:36 and
a VL as defined by SEQ ID NO:48,
vii) an scFv fragment having
a VH as defined by SEQ ID NO:37 and
15 a VL as defined by SEQ ID NO:49,
viii) an scFv fragment having
a VH as defined by SEQ ID NO:39 and
a VL as defined by SEQ ID NO:51,
ix) an scFv fragment having
20 a VH as defined by SEQ ID NO:40 and
a VL as defined by SEQ ID NO:52,
x) an scFv fragment having
a VH as defined by SEQ ID NO:41 and
a VL as defined by SEQ ID NO:53,
25 xi) an scFv fragment having
a VH as defined by SEQ ID NO:42 and
a VL as defined by SEQ ID NO:54,
xii) an scFv fragment having
a VH as defined by SEQ ID NO:43 and
30 a VL as defined by SEQ ID NO:55.

14. The human monoclonal antibody or antigen binding fragment thereof according to any one of claims 5-13, wherein the antibody or antigen binding fragment thereof is a synthetic scFv fragment having

- 35 CDR-H1 as defined by SEQ ID NO: 25
CDR-H2 as defined by SEQ ID NO: 26
CDR-H3 as defined by SEQ ID NO:4 and

CDR-L3 as defined by SEQ ID NO:16,
and wherein the scFv fragment bind a conglomerate comprising the proteins Isoform 12 of
Titin, Myosin-1, Myosin-2, Myosin-4, and Myosin-8.

5 15. An *in vitro* method for determining whether prostate cancer is present in a subject,
the method comprising:

 providing (S1) a human monoclonal antibody or antigen binding fragment
 thereof which selectively binds human prostasomes;

 reacting (S2) the human monoclonal antibody or antigen binding fragment
10 thereof with a sample comprising prostasomes from a subject;

 detecting (S3) any prostasomes bound by the human monoclonal antibody or
 antigen binding fragment thereof to obtain a level of prostasomes;

 comparing (S4) said level of prostasomes detected with a predetermined
 threshold; and

15 determining (S5) that prostate cancer is present in the subject if the detected level of
 prostasomes is higher than the predetermined threshold.

 16. The method according to claim 15, further comprising:

 determining (S5) that prostate cancer is not clinically detectable in the subject if the
20 detected level of prostasomes is lower than the predetermined threshold.

 17. The method according to claims 15-16, wherein detecting (S3) any prostasomes
 bound by the human monoclonal antibody or antigen binding fragment thereof comprises
 detecting the prostasomes using an anti-prostasome detection antibody or antigen binding
25 fragment thereof.

 18. The method according to claim 17, wherein the method is a sandwich
 immunoassay and detecting (S3) prostasomes (200) bound by the human monoclonal
 antibody or antigen binding fragment thereof (101) comprises detecting the anti-prostasome
30 detection antibody (102) using a further detection antibody (103), wherein the human
 monoclonal antibody or binding fragment thereof (101) is a capture antibody, the anti-
 prostasome detection antibody (102) is a primary detection antibody and the further detection
 antibody (103) is a secondary detection antibody.

35 19. The method according to claim 18, wherein the primary detection antibody (102) is
 a chicken antibody and the secondary detection antibody (103) is an anti-chicken antibody.

20. The method according to any one of claims 15-19, wherein the sample from the subject is a body fluid sample.

21. The method according to claim 20, wherein the body fluid sample from the subject
5 is selected from the group consisting of blood, serum, plasma, urine, cerebrospinal fluid and a cell suspension.

22. The method according to any one of claims 20-21, wherein the predetermined threshold is 10 ng prostasomes per mL of body fluid sample.

10

23. A method *in vitro* for providing a prognosis of a prostate cancer in a subject in need thereof, the method comprising:

providing (S11) a human monoclonal antibody or antigen binding fragment thereof which selectively binds prostasomes;

15

reacting (S12) the human monoclonal antibody or antigen binding fragment thereof with a sample from a subject comprising prostasomes;

detecting (S13) prostasomes bound by the human monoclonal antibody or antigen binding fragment thereof to obtain a level of prostasomes;

20

comparing (S14) said level of prostasomes detected with a first and second predetermined threshold; and

providing (S15) a prognosis of the prostate cancer, wherein prognosis of the prostate cancer is provided (S15a) to be poor if the detected level of prostasomes are above a first predetermined threshold, and provided (S15b) to be good if the detected level of prostasomes are below a second threshold.

25

24. The method according to claim 23, wherein the sample from the subject is a body fluid sample and wherein the first predetermined threshold is 10 ng prostasomes per mL of body fluid sample and the second predetermined threshold is 1 ng prostasomes per mL of body fluid sample.

30

25. A method *in vitro* for evaluating severity of a prostate cancer in a subject in need thereof, the method comprising:

providing (S21) a human monoclonal antibody or antigen binding fragment thereof which selectively binds prostasomes;

35

reacting (S22) the human monoclonal antibody or antigen binding fragment thereof with a sample from a subject comprising prostasomes;

detecting (S23) prostasomes bound by the human monoclonal antibody or antigen binding fragment thereof to obtain a level of prostasomes;

comparing (S24) said level of prostasomes detected with a first and second predetermined threshold; and

5 evaluating (S25) the severity of the prostate cancer, wherein the prostate cancer is evaluated (S25a) to be severe if the detected levels of prostasomes are above a first threshold, evaluated (S25b) to be moderate if the detected levels of prostasomes are below a first threshold but above a second threshold, and evaluated (S25c) to be light if the detected levels of prostasomes are below a second
10 threshold.

26. The method according to claim 25, wherein the sample from the subject is a body fluid sample and wherein the first predetermined threshold is 10 ng prostasomes per mL of body fluid sample and the second predetermined threshold is 1 ng prostasomes per mL of
15 body fluid sample.

27. A method *in vitro* of evaluating the efficacy of a prostate cancer treatment in a subject in need thereof, the method comprising:

20 detecting (S31) a level of prostasomes in a sample from a subject before a prostate cancer treatment;
 providing (S32) an anti-prostate cancer treatment to the subject;
 detecting (S33) a level of prostasomes in a sample from the subject after said prostate cancer treatment;
 comparing (S34) the level of prostasomes before the treatment to the levels
25 after the treatment; and
 determining (S35) the efficacy of the treatment, where the treatment is determined (S35a) to be effective if the level of prostasomes after the treatment have decreased compared to the level before the treatment, and determined (S35b) to be ineffective if the level of prostasomes have remained the same or increased, wherein detecting
30 (S31, S33) a level of prostasomes in a sample from a subject comprises:
 providing (S31a, S33a) a human monoclonal antibody or antigen binding fragment thereof which selectively binds prostasomes;
 reacting (S31b, S33b) the human monoclonal antibody or antigen binding fragment thereof with a sample from a subject comprising prostasomes; and
35 detecting (S31c, S33c) prostasomes bound by the human monoclonal antibody or antigen binding fragment thereof to obtain a level of prostasomes.

28. The method according to any one of claims 15-27, wherein the sample from the subject is a body fluid sample, selected from the group consisting of blood, serum, plasma, urine, cerebrospinal fluid and a cell suspension.

5

29. The method according to any one of claims 15-28, wherein the human monoclonal antibody or antigen binding fragment thereof is an antibody or antigen binding fragment thereof according to any one of claims 1-14.

10

30. Use of an antibody or antigen binding fragment thereof according to any one of claims 1-14 for use in the methods according to any one of claims 15-28.