

advantageous for detecting and quantifying GPC-1 levels in persons undergoing diagnostic and/or prognostic tests.

Summary

The present inventors have determined that a series of epitopes within the GPC-1 protein are preferably targeted by binding entities including, but not limited to, antibodies. In one aspect, the present invention relates to an isolated epitope or epitope segment for an anti-glypican 1 (GPC-1) antibody located within a portion of the GPC-1 flexible loop defined by an amino acid sequence KVNPGPGPEEK (**SEQ ID NO: 1**), wherein the isolated epitope or epitope segment consists of: (i) KVNPGPGPEEK (**SEQ ID NO: 1**); (ii) a fragment of KVNPGPGPEEK (**SEQ ID NO: 1**) consisting of VNPQGPPEEK (**SEQ ID NO: 2**), VNPQGPPEE (**SEQ ID NO: 3**), NPQGPPEE (**SEQ ID NO: 4**), KVNPGPGPE (**SEQ ID NO: 5**) or KVNPGPGP (**SEQ ID NO: 6**); (iii) a variant of **SEQ ID NO: 3** with a substitution at any one of: position 1, wherein V (val) is substituted with any other amino acid, position 2, wherein N (asn) is substituted with any other amino acid, position 3, wherein P (pro) is substituted with any other amino acid, position 4, wherein Q (gln) is substituted with any one of Y (tyr), A (ala), E (glu), V (val), M (met), F (phe), L (leu), I (ile), T (thr), or R (arg), position 5, wherein G (gly) is substituted with A (ala), S (ser), T (thr), H (his), W (trp), Y (tyr), F (phe), or M (met), position 8, wherein P (pro) is substituted with any other amino acid, or position 10, wherein E (glu) is substituted with Q (gln), D (asp), F (phe), H (his) or M (met), (iv) a variant of **SEQ ID NO: 4** with a substitution at any one of: position 1, wherein N (asn) is substituted with H (his), position 2, wherein P (pro) is substituted with any other amino acid, position 3, wherein Q (gln) is substituted with any one of N (asn), M (met), T (thr), S (ser), or R (arg), position 5, wherein P (pro) is substituted with A (ala), position 7, wherein P (pro) is substituted with any one of A (ala), D (asp), C (cys), E (glu), Z (glx), G (gly), H (his), K (lys), M (met), F (phe), P (pro), S (ser), T (thr), W (trp), or Y (tyr), or position 9, wherein E (glu) is substituted with any other amino acid; or (v) a variant of **SEQ ID NO: 5** or **SEQ ID NO: 6** with a substitution only at any one of: position 1, wherein K (lys) is substituted with any one of W (trp), R (arg), L (lys), Y (tyr) or F (phe); position 3, wherein N (asn) is substituted with any one of H (his), P (pro) or D (asp); position 4, wherein P (pro) is substituted with any one of R (arg), K (lys), W (trp), S (ser), H (his) or N (asn); position 8, wherein G (gly) is substituted with any one of D (asp), E (glu), N (asn), Q (gln), K (lys), R (arg) or A (ala); or position 9, wherein P (pro) is substituted with any one of M (met), A (ala), I (ile), K (lys), R (arg), Q (gln), S (ser), T (thr), or Y (tyr).

In another aspect, the present invention discloses an isolated epitope consisting of a first epitope segment as disclosed herein and a second segment, wherein: (i) the first segment is: the fragment of KVNPGQPGPEEK (**SEQ ID NO: 1**) consisting of VNPQGPPEEK (**SEQ ID NO: 2**), KVNPGPGPE (**SEQ ID NO: 5**) or KVNPGPGP (**SEQ ID NO: 6**); the variant of KVNPGPGPE (**SEQ ID NO: 5**); or the variant of KVNPGPGP (**SEQ ID NO: 6**); and(ii) the second segment consists of an amino acid sequence TQNARA (**SEQ ID NO: 8**).

In yet another aspect, the present invention refers to an isolated epitope consisting of a first epitope segment as disclosed herein and a second segment, wherein: (i) the first segment is: the fragment of KVNPGQPGPEEK (**SEQ ID NO: 1**) consisting of NPQGPPEE (**SEQ ID NO: 4**); or the variant of NPQGPPEE (**SEQ ID NO: 4**); and (ii) the second segment consists of an amino acid sequence ALSTASDDR (**SEQ ID NO: 9**).

In yet another aspect, the present invention refers to an isolated epitope consisting of a first epitope segment as disclosed herein and a second segment, wherein: (i) the first segment is: the fragment of KVNPGQPGPEEK (**SEQ ID NO: 1**) consisting of VNPQGPPEE (**SEQ ID NO: 3**); and (ii) the epitope second segment consists of: an amino acid sequence PRERPP (**SEQ ID NO: 10**) or an amino acid sequence QDASDDGSGS (**SEQ ID NO: 11**).

In yet another aspect, the present invention refers to an isolated epitope consisting of a first epitope segment according to claim 1, a second segment, and a third segment wherein: (i) the first segment is: the fragment of KVNPGQPGPEEK (**SEQ ID NO: 1**) consisting of VNPQGPPEE (**SEQ ID NO: 3**); and (ii)the second segment consists of an amino acid sequence PRERPP (**SEQ ID NO: 10**), and the third segment consists of an amino acid sequence QDASDDGSGS (**SEQ ID NO: 11**).

In yet another aspect, the present invention refers to an isolated epitope comprising the epitope segment as disclosed herein and consisting of the amino acid sequence CGELYTQNARAFRDLCGNPKVNPGQPGPEEKRRRGK (**SEQ ID NO: 12**).

In yet another aspect, the present invention refers to an isolated epitope or epitope segment for an anti-glypican 1 (GPC-1) antibody consisting of an amino acid sequence selected from any one or a plurality of: TQNARA (**SEQ ID NO: 8**), ALSTASDDR (**SEQ ID NO: 9**), PRERPP (**SEQ ID NO: 10**), QDASDDGSGS (**SEQ ID NO: 11**), LGPECSRAVMK (**SEQ ID NO: 13**), and TQNARAFRD (**SEQ ID NO: 7**).

In yet another aspect, the present invention refers to an arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein each said distinct epitope is an epitope as disclosed herein.

In yet another aspect, the present invention refers to an arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein the arrangement comprises a first epitope as disclosed herein, and a second epitope as disclosed herein.

In yet another aspect, the present invention refers to a composition comprising an epitope as disclosed herein, or an arrangement of epitopes as disclosed herein, and a pharmaceutically acceptable carrier or excipient.

In yet another aspect, the present invention refers to an assembly comprising an epitope as disclosed herein, or an arrangement of epitopes as disclosed herein, bound to one or more soluble or insoluble supports.

In yet another aspect, the present invention refers to a nucleic acid encoding the epitope as disclosed herein.

In yet another aspect, the present invention refers to a vector comprising the nucleic acid as disclosed herein.

In yet another aspect, the present invention refers to a host cell comprising the vector as disclosed herein.

In yet another aspect, the present invention refers to an isolated binding entity capable of specifically binding to an epitope as disclosed herein, wherein the binding entity is not an antibody.

In yet another aspect, the present invention refers to an isolated binding entity capable of specifically binding to an epitope as disclosed herein, wherein the binding entity is an antibody and with the proviso that the antibody is not a: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

In yet another aspect, the present invention refers to a method for detecting prostate cancer in a subject, the method comprising detecting the presence of an as disclosed herein in a biological sample obtained from the subject, and determining that the subject has prostate cancer or an increased likelihood of developing prostate cancer based on amount of the epitope detected in the sample.

In yet another aspect, the present invention refers to a fusion protein comprising the epitope as disclosed herein.

In yet another aspect, the present invention refers to use of the epitope as disclosed herein, the arrangement of epitopes as disclosed herein, or the fusion protein as disclosed herein, as a positive control element in a method for detecting GPC-1.

Accordingly, the present disclosure relates to at least the following examples :

Example 1: An epitope for an anti-glypican 1 (GPC-1) antibody located within a portion of the GPC-1 flexible loop defined by an amino acid sequence KVNPGPGPEEK (**SEQ ID NO: 1**).

Example 2: The epitope according to example 1, wherein the epitope comprises a first segment comprising an amino acid sequence selected from:

- (i) VNPQGPPEEK (**SEQ ID NO: 2**); or
- (ii) a variant of VNPQGPPEEK (**SEQ ID NO: 2**), wherein the variant comprises a substituted amino acid residue only at:

any one or more of positions 2, 3, 7, 8, 9, 10 and/or 11; or

any one or more of positions 1, 2, 3, 4, 6, 8, 10 and/or 11; or

any one or more of positions 1, 2, 3, 4, 5, 8, 10 and/or 11.

Example 3: The epitope according to example 1 wherein the epitope comprises a first segment comprising an amino acid sequence selected from:

- (i) KVNPGPGP (**SEQ ID NO: 6**); or
- (ii) a variant of KVNPGPGP (**SEQ ID NO: 6**) comprising a substituted amino acid residue only at any one or more of positions 1, 3, 4, 8, and 9 of **SEQ ID NO: 6**.

Example 4: The variant according to example 3, comprising a substituted amino acid residue only at any one or more of positions 8 and 9 of **SEQ ID NO: 6**.

Example 5: The epitope according to example 1, wherein the epitope comprises a first segment comprising an amino acid sequence selected from:

- (i) KVNPGPGPE (**SEQ ID NO: 5**); or
- (ii) a variant of KVNPGPGPE (**SEQ ID NO: 5**) comprising a substituted amino acid residue only at any one or more of positions 1, 3, 4, 8, 9 and 10 of **SEQ ID NO: 5**.

Example 6: The variant according to example 5, comprising a substituted amino acid residue only at any one or more of positions 8, 9 and 10 of **SEQ ID NO: 6**.

Example 7: The variant according to example 5 or example 6, wherein E (glu) at position 10 is substituted with any other amino acid.

Example 8: The variant according to any one of examples 3 to 7, wherein the variant comprises a substitution only at any one or more of:

position 1, wherein K (lys) is substituted with any one of W (trp), R (arg), L (lys), Y (tyr) or F (phe);

position 3, wherein N (asn) is substituted with any one of H (his), P (pro) or D (asp);

position 4, wherein P (pro) is substituted with any one of R (arg), K (lys), W (trp), S (ser), H (his) or N (asn);

position 8, wherein G (gly) is substituted with any one of D (asp), E (glu), N (asn), Q (gln), K (lys), R (arg) or A (ala);

position 9, wherein P (pro) is substituted with any one of M (met), A (ala), I (ile), K (lys), R (arg), Q (gln), S (ser), T (thr), or Y (tyr).

Example 9: The epitope according to any one of examples 1 to 8, comprising a second segment comprising an amino acid sequence TQNARA (**SEQ ID NO: 8**).

Example 10: The epitope according to any one of examples 1 to 8, comprising a second segment comprising an amino acid sequence TQNARAFRD (**SEQ ID NO: 7**).

Example 11: The epitope according to example 1 or example 2, wherein the epitope comprises a first segment comprising an amino acid sequence selected from:

(i) NPQGGPGPEE (**SEQ ID NO: 4**); or

(ii) a variant of NPQGGPGPEE (**SEQ ID NO: 4**), wherein the variant comprises a substituted amino acid residue only at any one or more of positions 1, 2, 3, 5, 7 and 9 of **SEQ ID NO: 4**.

Example 12: The variant according to example 11, comprising a substituted amino acid residue only at any one or more of positions 2, 7, and 9 of **SEQ ID NO: 4**.

Example 13: The variant according to example 11 or example 12, wherein the variant comprises a substitution at any one or more of:

position 1, wherein N (asn) is substituted with H (his);

position 2, wherein P (pro) is substituted with any other amino acid;

position 3, wherein Q (gln) is substituted with any one of N (asn), M (met), T (thr), S (ser), or R (arg);

position 5, wherein P (pro) is substituted with A (ala);

position 7, wherein P (pro) is substituted with any one of A (ala), D (asp), C (cys), E (glu), Z (glx), G (gly), H (his), K (lys), M (met), F (phe), P (pro), S (ser), T (thr), W (trp), or Y (tyr);

position 9, wherein E (glu) is substituted with any other amino acid.

Example 14: The epitope according to any one of examples 11 to 13, wherein the epitope comprises a second segment comprising an amino acid sequence ALSTASDDR (**SEQ ID NO: 9**).

Example 15: The epitope according to example 1 or example 2, wherein the epitope comprises a first segment comprising an amino acid sequence selected from:

(i) VNPQGGPGPEE (**SEQ ID NO: 3**); or

(ii) a variant of VNPQGPGE (SEQ ID NO: 3), wherein the variant comprises a substituted amino acid residue only at any one or more of positions 1, 2, 3, 4, 5, 8 and 10 of SEQ ID NO: 3.

Example 16: The variant according to example 15, comprising a substituted amino acid residue only at any one or more of positions 1, 2, 3, and 8 of SEQ ID NO: 3.

Example 17: The variant according to example 15 or example 16, wherein the variant comprises a substitution at any one or more of:

position 1, wherein V (val) is substituted with any other amino acid;

position 2, wherein N (asn) is substituted with any other amino acid;

position 3, wherein P (pro) is substituted with any other amino acid;

position 4, wherein Q (gln) is substituted with any one of Y (tyr), A (ala), E (glu), V (val), M (met), F (phe), L (leu), I (ile), T (thr), or R (arg);

position 5, wherein G (gly) is substituted with A (ala), S (ser), T (thr), H (his), W (trp), Y (tyr), F (phe), or M (met);

position 8, wherein P (pro) is substituted with any other amino acid;

position 10, wherein E (glu) is substituted with Q (gln), D (asp), F (phe), H (his) or M (met).

Example 18: The epitope according to any one of examples 15 to 17, wherein the epitope comprises a second segment comprising:

an amino acid sequence PRERPP (SEQ ID NO: 10) or

an amino acid sequence QDASDDGSGS (SEQ ID NO: 11).

Example 19: The epitope according to any one of examples 15 to 17, wherein the epitope comprises a second segment comprising an amino acid sequence PRERPP (SEQ ID NO: 10) and a third segment comprising an amino acid sequence QDASDDGSGS (SEQ ID NO: 11).

Example 20: The epitope according to any one of examples 1 to 10, comprising the amino acid sequence CGELYTQNARAFRDLCGNPKVNPQGPGEKRRRG (SEQ ID NO: 12).

Example 21: The epitope according to any one of examples 1 to 20, wherein the epitope is a linear epitope.

Example 22: The epitope according to example 19, wherein the second segment and the third segment of the epitope are discontinuous.

Example 23: The epitope according to any one of examples 9, 10, 14, 18 or 22 wherein the first segment and the second segment of the epitope are discontinuous.

Example 24: An epitope for an anti-glypican 1 (GPC-1) antibody comprising an amino acid sequence selected from any one or a plurality of: TQNARA (**SEQ ID NO: 8**), ALSTASDDR (**SEQ ID NO: 9**), PRERPP (**SEQ ID NO: 10**), QDASDDGSGS (**SEQ ID NO: 11**), LGPECSRAVMK (**SEQ ID NO: 13**), and TQNARAFRD (**SEQ ID NO: 7**).

Example 25: The epitope according to any one of examples 1 to 24, wherein the epitope is an isolated polypeptide or a synthetic polypeptide.

Example 26: An arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein

each said distinct epitope is an epitope according to any one of examples 1 to 25;

each said epitope is an epitope according to **Table 1**; or

the combination of epitopes is any one or more of the combinations set out in **Table 3**.

Example 27: An arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein the arrangement comprises

a first epitope according to any one of examples 1 to 10, and

a second epitope according to any one of examples 11 to 14.

Example 28: An arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein the arrangement comprises

a first epitope according to any one of examples 1 to 10, and

a second epitope according to any one of examples 15 to 19.

Example 29: A composition comprising an epitope according to any one of examples 1 to 25, or an arrangement of epitopes according to any one of examples 26 to 28, and a pharmaceutically acceptable carrier or excipient.

Example 30: An assembly comprising an epitope according to any one of examples 1 to 25, or an arrangement of epitopes according to any one of examples 26 to 28, bound to one or more soluble or insoluble supports.

Example 31: The assembly of example 30, wherein the assembly is a component of an enzyme-linked immunosorbent assay (ELISA).

Example 32: A nucleic acid encoding the epitope according to any one of examples 1 to 25.

Example 33: A vector comprising the nucleic acid according to example 32.

Example 34: A host cell comprising the vector according to example 33.

Example 35: An isolated binding entity capable of specifically binding to an epitope according to any one of examples 1 to 25, wherein the binding entity is not an antibody.

Example 36: An isolated binding entity capable of specifically binding to an epitope according to any one of examples 1 to 25, wherein the binding entity is an antibody and with the proviso that the antibody is not a: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

Example 37: A method for detecting prostate cancer in a subject, the method comprising obtaining a biological sample from the subject, detecting the presence of an epitope according to any one of examples 1 to 25 in the sample, and determining that the subject has prostate cancer or an increased likelihood of developing prostate cancer based on amount of the epitope detected in the sample.

The biological sample may be a body fluid sample.

The biological sample may be a tissue sample.

Example 38: The method according to example 37, wherein detecting the presence of the epitope in the sample comprises contacting the sample with a binding entity capable of specifically binding to an epitope according to any one of examples 1 to 25.

Example 39: The method according to example 38, wherein the binding entity is a population of antibodies.

Example 40: The method according to example 39, wherein the population of antibodies comprises any one or more of: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

Example 41: The method according to example 39, wherein the population of antibodies does not contain any of: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

Example 42: The method according to any one of examples 37 to 41, comprising comparing the amount of epitope present in the biological sample with an amount of epitope present in a control sample, wherein the detection of an increased amount of epitope in the body fluid sample compared to an equivalent measure of the control sample is indicative of prostate cancer in the subject or an increased likelihood of developing prostate cancer in the subject.

Example 43: The method according to example 42, wherein the amount of epitope detected in the sample is increased by more than 50% over the amount of epitope detected in the control sample.

Example 44: The method according to any one of examples 37 to 43, wherein detecting the presence of the epitope comprises contacting the sample with a population of MIL38 antibodies as deposited at Cellbank Australia under accession number CBA20140026.

Example 45: The method according to any one of examples 37 to 43, wherein detecting the presence of the epitope comprises contacting the sample with a population of antibodies that does not comprise an antibody comprising a light chain variable region comprising: a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 48-58 of **SEQ ID NO: 20**; a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 74-80 of **SEQ ID NO: 20**; and/or a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 113-121 of **SEQ ID NO: 20**.

Example 46: The method according to any one of examples 37 to 45, further comprising determining the level of prostate-specific antigen (PSA) in the biological sample and comparing the level detected to that of the control sample.

Example 47: The method according to any one of examples 37 to 46, wherein the biological sample is a body fluid sample.

Example 48: The method according to any one of examples 37 to 46, wherein the biological sample is a tissue sample.

Example 49: A fusion protein comprising the epitope according to any one of examples 1 to 25.

Example 50: Use of the epitope according to any one of examples 1 to 25, the arrangement of epitopes according to any one of examples 26 to 28, or the fusion protein according to example 48, as a positive control element in a method for detecting GPC-1.

Example 51: The use according to example 50, wherein the method is the method for detecting prostate cancer according to any one of examples 37 to 48.

Claims

1. An isolated epitope or epitope segment for an anti-glypican 1 (GPC-1) antibody located within a portion of the GPC-1 flexible loop defined by an amino acid sequence KVN PQGP GPEEK (**SEQ ID NO: 1**), wherein the isolated epitope or epitope segment consists of:

- (i) KVN PQGP GPEEK (**SEQ ID NO: 1**);
- (ii) a fragment of KVN PQGP GPEEK (**SEQ ID NO: 1**) consisting of VNP QGP GPEEK (**SEQ ID NO: 2**), VNP QGP GPEE (**SEQ ID NO: 3**), NP QGP GPEE (**SEQ ID NO: 4**), KVN PQGP GPE (**SEQ ID NO: 5**) or KVN PQGP GP (**SEQ ID NO: 6**);
- (iii) a variant of **SEQ ID NO: 3** with a substitution at any one of:
 - position 1, wherein V (val) is substituted with any other amino acid,
 - position 2, wherein N (asn) is substituted with any other amino acid,
 - position 3, wherein P (pro) is substituted with any other amino acid,
 - position 4, wherein Q (gln) is substituted with any one of Y (tyr), A (ala), E (glu), V (val), M (met), F (phe), L (leu), I (ile), T (thr), or R (arg),
 - position 5, wherein G (gly) is substituted with A (ala), S (ser), T (thr), H (his), W (trp), Y (tyr), F (phe), or M (met),
 - position 8, wherein P (pro) is substituted with any other amino acid, or
 - position 10, wherein E (glu) is substituted with Q (gln), D (asp), F (phe), H (his) or M (met),
- (iv) a variant of **SEQ ID NO: 4** with a substitution at any one of:
 - position 1, wherein N (asn) is substituted with H (his),
 - position 2, wherein P (pro) is substituted with any other amino acid,
 - position 3, wherein Q (gln) is substituted with any one of N (asn), M (met), T (thr), S (ser), or R (arg),
 - position 5, wherein P (pro) is substituted with A (ala),
 - position 7, wherein P (pro) is substituted with any one of A (ala), D (asp), C (cys), E (glu), Z (glx), G (gly), H (his), K (lys), M (met), F (phe), P (pro), S (ser), T (thr), W (trp), or Y (tyr), or
 - position 9, wherein E (glu) is substituted with any other amino acid; or
- (v) a variant of **SEQ ID NO: 5** or **SEQ ID NO: 6** with a substitution only at any one of:
 - position 1, wherein K (lys) is substituted with any one of W (trp), R (arg), L (lys), Y (tyr) or F (phe);
 - position 3, wherein N (asn) is substituted with any one of H (his), P (pro) or D (asp);

position 4, wherein P (pro) is substituted with any one of R (arg), K (lys), W (trp), S (ser), H (his) or N (asn);

position 8, wherein G (gly) is substituted with any one of D (asp), E (glu), N (asn), Q (gln), K (lys), R (arg) or A (ala); or

position 9, wherein P (pro) is substituted with any one of M (met), A (ala), I (ile), K (lys), R (arg), Q (gln), S (ser), T (thr), or Y (tyr).

2. An isolated epitope consisting of a first epitope segment according to claim 1 and a second segment, wherein:

(i) the first segment is: the fragment of KVNPPQGGPPEEK (**SEQ ID NO: 1**) consisting of VNPQGGPPEEK (**SEQ ID NO: 2**), KVNPPQGGPPE (**SEQ ID NO: 5**) or KVNPPQGGPP (**SEQ ID NO: 6**); the variant of VNPQGGPPEEK (**SEQ ID NO: 2**); the variant of KVNPPQGGPPE (**SEQ ID NO: 5**); or the variant of KVNPPQGGPP (**SEQ ID NO: 6**); and

(ii) the second segment consists of an amino acid sequence TQNARA (**SEQ ID NO: 8**).

3. The epitope according to claim 2, wherein the second segment consists of an amino acid sequence TQNARAFRD (**SEQ ID NO: 7**).

4. An isolated epitope consisting of a first epitope segment according to claim 1 and a second segment, wherein:

(i) the first segment is: the fragment of KVNPPQGGPPEEK (**SEQ ID NO: 1**) consisting of NPQGGPPEE (**SEQ ID NO: 4**); or the variant of NPQGGPPEE (**SEQ ID NO: 4**); and

(ii) the second segment consists of an amino acid sequence ALSTASDDR (**SEQ ID NO: 9**).

5. An isolated epitope consisting of a first epitope segment according to claim 1 and a second segment, wherein:

(i) the first segment is: the fragment of KVNPPQGGPPEEK (**SEQ ID NO: 1**) consisting of VNPQGGPPEE (**SEQ ID NO: 3**); and

(ii) the epitope second segment consists of:

an amino acid sequence PRERPP (**SEQ ID NO: 10**) or

an amino acid sequence QDASDDGSGS (**SEQ ID NO: 11**).

6. An isolated epitope consisting of a first epitope segment according to claim 1, a second segment, and a third segment wherein:

(i) the first segment is: the fragment of KVNPGPGPEEK (**SEQ ID NO: 1**) consisting of VNPQGPPEE (**SEQ ID NO: 3**); and

(ii) the second segment consists of an amino acid sequence PRERPP (**SEQ ID NO: 10**), and the third segment consists of an amino acid sequence QDASDDGSGS (**SEQ ID NO: 11**).

7. An isolated epitope comprising the epitope segment according to claim 1 and consisting of the amino acid sequence CGELYTQNARAFRDLCGNPKVNPGPGPEEKRRRGC (**SEQ ID NO: 12**).

8. The epitope according to claim 1, wherein the epitope is a linear epitope.

9. The epitope according to claim 6, wherein the second segment and the third segment of the epitope are discontinuous.

10. The epitope according to any one of claims 2 to 5 or 9, wherein the first segment and the second segment of the epitope are discontinuous.

11. An isolated epitope or epitope segment for an anti-glypican 1 (GPC-1) antibody consisting of an amino acid sequence selected from any one or a plurality of: TQNARA (**SEQ ID NO: 8**), ALSTASDDR (**SEQ ID NO: 9**), PRERPP (**SEQ ID NO: 10**), QDASDDGSGS (**SEQ ID NO: 11**), LGPECSRAVMK (**SEQ ID NO: 13**), and TQNARAFRD (**SEQ ID NO: 7**).

12. The epitope or epitope segment according to any one of claims 1 to 11, wherein the epitope is a synthetic polypeptide.

13. An arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein each said distinct epitope is an epitope according to any one of claims 1 to 12.

14. An arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein the arrangement comprises

a first epitope according to claim 2, and

a second epitope according to claim 3.

15. An arrangement of epitopes comprising a combination of two or more distinct epitopes, wherein the arrangement comprises
a first epitope according to claim 2, and
a second epitope according to claim 4 or claim 5.

16. A composition comprising an epitope according to any one of claims 1 to 12, or an arrangement of epitopes according to any one of claims 13 to 15, and a pharmaceutically acceptable carrier or excipient.

17. An assembly comprising an epitope according to any one of claims 1 to 12, or an arrangement of epitopes according to any one of claims 13 to 15, bound to one or more soluble or insoluble supports.

18. The assembly of claim 17, wherein the assembly is a component of an enzyme-linked immunosorbent assay (ELISA).

19. A nucleic acid encoding the epitope according to any one of claims 1 to 12.

20. A vector comprising the nucleic acid according to claim 19.

21. A host cell comprising the vector according to claim 20.

22. An isolated binding entity capable of specifically binding to an epitope according to any one of claims 1 to 12, wherein the binding entity is not an antibody.

23. An isolated binding entity capable of specifically binding to an epitope according to any one of claims 1 to 12, wherein the binding entity is an antibody and with the proviso that the antibody is not a: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

24. A method for detecting prostate cancer in a subject, the method comprising detecting the presence of an epitope according to any one of claims 1 to 12 in a biological sample obtained from the subject, and determining that the subject has prostate cancer or an

increased likelihood of developing prostate cancer based on amount of the epitope detected in the sample.

25. The method according to claim 24, wherein detecting the presence of the epitope in the sample comprises contacting the sample with a binding entity capable of specifically binding to an epitope according to any one of claims 1 to 12.

26. The method according to claim 25, wherein the binding entity is a population of antibodies.

27. The method according to claim 26, wherein the population of antibodies comprises any one or more of: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

28. The method according to claim 26, wherein the population of antibodies does not contain any of: MIL38 antibody (CBA20140026), rabbit anti-GPC-1 polyclonal antibody (ab137604, abcam), mouse anti-glypican monoclonal antibody 2600 clone 4D1 (Millipore), or goat anti-glypican 1 antibody (AA 24-530).

29. The method according to any one of claims 24 to 28, comprising comparing the amount of epitope present in the biological sample with an amount of epitope present in a control sample, wherein the detection of an increased amount of epitope in the body fluid sample compared to an equivalent measure of the control sample is indicative of prostate cancer in the subject or an increased likelihood of developing prostate cancer in the subject.

30. The method according to claim 29, wherein the amount of epitope detected in the sample is increased by more than 50% over the amount of epitope detected in the control sample.

31. The method according to any one of claims 24 to 30, wherein detecting the presence of the epitope comprises contacting the sample with a population of MIL38 antibodies as deposited at Cellbank Australia under accession number CBA20140026.

32. The method according to any one of claims 24 to 30, wherein detecting the presence of the epitope comprises contacting the sample with a population of anti-glypican 1

antibodies that does not comprise an antibody comprising a light chain variable region comprising: a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 48-58 of **SEQ ID NO: 20**; a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 74-80 of **SEQ ID NO: 20**; a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 113-121 of **SEQ ID NO: 20**.

33. The method according to any one of claims 24 to 32, further comprising determining the level of prostate-specific antigen (PSA) in the biological sample and comparing the level detected to that of the control sample.

34. The method according to any one of claims 24 to 33, wherein the biological sample is a body fluid sample.

35. The method according to any one of claims 24 to 33, wherein the biological sample is a tissue sample.

36. A fusion protein comprising the epitope according to any one of claims 1 to 12.

37. Use of the epitope according to any one of claims 1 to 12, the arrangement of epitopes according to any one of claims 13 to 15, or the fusion protein according to claim 36, as a positive control element in a method for detecting GPC-1.

38. The use according to claim 37, wherein the method is the method for detecting prostate cancer according to any one of claims 24 to 35.