

delivery of a heterologous cargo moiety. There also remains a need for anti-TAT antibodies to be used for therapeutic purposes in the treatment of HIV infection.

SUMMARY

5 In certain examples, the present disclosure provides for anti-TAT binding proteins, e.g., antibodies, and antigen binding portions thereof, that bind to a TAT protein transduction domain.

 In one aspect, the present disclosure provides a binding protein comprising an antigen binding domain, the antigen binding domain comprising a heavy chain CDR3
10 domain comprising the amino acid sequence of SEQ ID NO: 4, wherein the binding protein is capable of binding a TAT protein transduction domain.

 In some examples, the antigen binding domain further comprises a heavy chain CDR2 domain comprising the amino acid sequence of SEQ ID NO: 3.

 In some examples, the antigen binding domain further comprises a heavy chain
15 CDR1 domain comprising the amino acid sequence of SEQ ID NO: 2.

 In some examples, the antigen binding domain further comprises a light chain CDR3 domain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 8 and SEQ ID NO: 12.

 In some examples, the antigen binding domain further comprises a light chain
20 CDR2 domain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 7 and SEQ ID NO: 11.

 In some examples, the antigen binding domain further comprises a light chain CDR1 domain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 10.

25 In another aspect, the present disclosure provides a binding protein comprising an antigen binding domain, the antigen binding domain comprising: a heavy chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 3, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 2;
30 and a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6; or a light chain variable region comprising a CDR3

domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10, wherein the binding protein is capable of binding a TAT protein transduction domain.

5 In some examples, the antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 14.

 In some examples, the antigen binding domain comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5, a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9, or a light
10 chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 13.

 In some examples, the antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5.

 In some examples, the antigen binding domain comprises a heavy chain variable
15 region comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9.

 In some examples, the antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 13.

20 In some examples, the antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 14 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5.

 In another aspect, the present disclosure provides a binding protein comprising an antigen binding domain, the antigen binding domain comprising a heavy chain CDR3
25 domain comprising the amino acid sequence of SEQ ID NO: 18, wherein the binding protein is capable of binding a TAT protein transduction domain.

 In some examples, the antigen binding domain further comprises a heavy chain CDR2 domain comprising the amino acid sequence of SEQ ID NO: 17.

 In some examples, the antigen binding domain further comprises a heavy chain
30 CDR1 domain comprising the amino acid sequence of SEQ ID NO: 16.

In some examples, the antigen binding domain further comprises a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 22.

In some examples, the antigen binding domain further comprises a light chain CDR2 domain comprising the amino acid sequence of SEQ ID NO: 21.

5 In some examples, the antigen binding domain further comprises a light chain CDR1 domain comprising the amino acid sequence of SEQ ID NO: 20.

In another aspect, the present disclosure provides a binding protein comprising an antigen binding domain, the antigen binding domain comprising: a heavy chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ
10 ID NO: 18, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 17, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 16; and a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 22, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 21, and a CDR1 domain comprising the amino acid
15 sequence set forth in SEQ ID NO: 20, wherein the binding protein is capable of binding a TAT protein transduction domain.

In some examples, the antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 15.

In some examples, the antigen binding domain comprises a light chain variable
20 region comprising the amino acid sequence set forth in SEQ ID NO: 19.

In some examples, the antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 15 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 19.

In some examples, the TAT protein transduction domain comprises the amino acid
25 sequence of SEQ ID NO: 23.

In some examples, the TAT protein transduction domain consists essentially of the amino acid sequence of SEQ ID NO: 23.

In some examples, the TAT protein transduction domain is covalently linked to a cargo moiety.

30 In some examples, the cargo moiety is a polypeptide.

In some examples, the cargo moiety is a frataxin polypeptide.

In some examples, the cargo moiety is an antibody.

In some examples, the cargo moiety is a nucleic acid. In some examples, the nucleic acid is an siRNA, shRNA, miRNA, phosphorothioate modified RNA, aptamer, phosphorodiamidate morpholino oligomer (PMO), or any combination thereof.

5 In some examples, the cargo moiety is a small molecule, a liposome enclosing protein, a radionuclide or radionuclide labeled compound, or any combination thereof.

In some examples, the binding protein is capable of binding to a TAT protein transduction domain that is covalently linked to a cargo moiety.

10 In another aspect, the present disclosure provides a binding protein comprising an antigen binding domain, wherein said binding protein is capable of binding to a TAT protein transduction domain that is covalently linked to a cargo moiety.

In some examples, the antigen binding domain binds to an epitope comprising the amino acid residues of SEQ ID NO: 23.

In some examples, a binding protein disclosed herein is an antibody.

15 In another aspect, the present disclosure provides an antibody construct comprising a binding protein of the disclosure, further comprising a linker polypeptide or an immunoglobulin constant domain.

20 In some examples, binding protein is selected from the group consisting of: an immunoglobulin molecule, a monoclonal antibody, a murine antibody, a chimeric antibody, a CDR-grafted antibody, a humanized antibody, a single domain antibody, a Fv, a disulfide linked Fv, a scFv, a diabody, a Fab, a Fab', a F(ab')₂, a multispecific antibody, a dual specific antibody, and a bispecific antibody.

25 In some examples, the antibody construct comprises a binding protein which comprises a heavy chain immunoglobulin constant domain selected from the group consisting of: a IgM constant domain, a IgG₄ constant domain, a IgG₁ constant domain, a IgE constant domain, a IgG₂ constant domain, a IgG₃ constant domain and a IgA constant domain.

In some examples, the heavy chain immunoglobulin constant domain is not IgM.

In another aspect, the present disclosure provides an isolated nucleic acid encoding a binding protein amino acid sequence of the disclosure.

30 In another aspect, the present disclosure provides an isolated nucleic acid encoding an antibody construct amino acid sequence of the disclosure.

In another aspect, the present disclosure provides a vector comprising an isolated nucleic acid as described herein; optionally wherein said vector is selected from the group

consisting of pcDNA, pTT, pTT3, pEFBOS, pBV, pJV, pBJ, pGEX, VSV, pBR322, pCMV-HA, pEN, YAC,

BAC, Bacteriophage Lamda, Phagemid, pCAS9, pCEN6, pYES1L, p3HPRT1, pFN2A, pBC, pTZ, pGEM, pGEMK, pEX, pSAR, pCEP, Cosmids, pBluescript, pKJK, pFloxin, pCP, pHR, pUC, and pMAL.

5 In another example, the present disclosure provides a vector comprising an isolated nucleic acid according to the disclosure.

In some examples, the vector is selected from the group consisting of pcDNA, pTT, pTT3, pEFBOS, pBV, pJV, pBJ, pGEX, VSV, pBR322, pCMV-HA, pEN, YAC, BAC, Bacteriophage Lamda, Phagemid, pCAS9, pCEN6, pYES1L, p3HPRT1, pFN2A, pBC, pTZ, pGEM, pGEMK, pEX, pSAR, pCEP, Cosmids, pBluescript, pKJK, pFloxin,
10 pCP, pHR, pUC, and pMAL.

In another aspect, the present disclosure provides a host cell comprising a vector as described herein; optionally wherein said host cell is a prokaryotic cell or a eukaryotic cell, or wherein said host cell is selected from the group consisting of a CHO cell, a COS cell, a yeast cell, an insect Sf9 cell, HEK-293 cell, ExpiCHO cell, Expi-293f cell, and
15 *E. Coli* cell; further optionally: (a) wherein said prokaryotic host cell is *E. Coli*; or (b) wherein said eukaryotic host cell is selected from the group consisting of a protist cell, an insect cell, an animal cell, a plant cell and a fungal cell, further optionally wherein said animal cell is a mammalian cell or an avian cell; or (c) wherein said yeast cell is *Saccharomyces cerevisiae*.

20 In another example, the present disclosure provides a host cell comprising a vector according to the disclosure.

In some examples, the host cell is a prokaryotic cell or a eukaryotic cell. In some examples, the prokaryotic host cell is *E. Coli*. In some examples, the eukaryotic cell is selected from the group consisting of a protist cell, an insect cell, an animal cell, a plant
25 cell and a fungal cell. In some examples, the animal cell is a mammalian cell or an avian cell. In some examples, the host cell is selected from the group consisting of a CHO cell, a COS cell, a yeast cell, an insect Sf9 cell, HEK-293 cell, ExpiCHO cell, Expi-293f cell, and *E. Coli* cell. In some examples, the yeast cell is *Saccharomyces cerevisiae*.

In another aspect, the present disclosure provides a method of producing an
30 antibody, or antigen binding portion thereof, comprising culturing the host cell in culture medium so that the isolated nucleic acid is expressed and the antibody is produced.

In another aspect, the present disclosure provides an antibody produced according to the methods of the disclosure.

In another aspect, the present disclosure provides a transgenic mouse comprising the host cell described herein, wherein the mouse expresses a polypeptide encoded by the nucleic acid, or an antigen binding portion thereof, that binds to a TAT protein transduction domain.

5 In another aspect, the present disclosure provides a hybridoma that produces the antibody construct described herein.

 In some examples, a binding protein according to the disclosure is immobilized on a solid support. In some examples, the solid support is a plate, a bead, or a chromatography resin. In some examples, the bead or chromatography resin comprises
10 protein A agarose or protein G agarose.

 In some examples, the binding protein of the disclosure is conjugated to a detection molecule.

 In some examples, the detection molecule is horseradish peroxidase, sulfotag, alkaline phosphatase, cresol violet, quantum dots, FITC, an infrared molecule, a
15 radiolabel, or an EPR spin tracer label.

In another aspect, the present disclosure provides a method for detecting and/or quantifying the level of a TAT fusion molecule in a sample, comprising contacting the sample with a binding protein of the disclosure under conditions such that the binding protein binds to TAT protein transduction domain in the sample, to thereby detect and/or
5 quantify the level of the TAT fusion molecule in the sample.

In some examples, the sample is a biological sample.

In some examples, the biological sample is a liquid sample or a tissue sample.

In some examples, the TAT fusion molecule comprises a TAT protein transduction domain covalently linked to a cargo moiety.

10 In some examples, the cargo moiety is a polypeptide.

In some examples, the cargo moiety is a frataxin polypeptide.

In some examples, the cargo moiety is an antibody.

In some examples, the cargo moiety is a nucleic acid. In some examples, the nucleic acid is an siRNA, shRNA, miRNA, phosphorothioate modified RNA, aptamer,
15 phosphorodiamidate morpholino oligomer (PMO), or any combination thereof.

In some examples, the cargo moiety is a small molecule, a liposome enclosing protein, a radionuclide or radionuclide labeled compound, or any combination thereof.

In some examples, the stability of the TAT fusion molecule is assessed.

In another aspect, the present disclosure provides a method of isolating and/or
20 purifying a TAT fusion molecule present in a mixture, wherein the TAT fusion molecule comprises a TAT protein transduction domain covalently linked to a cargo moiety, comprising (a) contacting the mixture comprising the TAT fusion molecule with the immobilized binding protein of the disclosure under conditions such that the TAT fusion molecule binds to the immobilized binding protein; (b) eluting the TAT fusion molecule
25 from the immobilized binding protein.

In another aspect, the present disclosure provides a kit comprising at least one reagent specific for the detection of a level of a TAT protein transduction domain, wherein the detection reagent is a binding protein as described herein, optionally: wherein the TAT protein transduction domain is covalently linked to a cargo moiety and/or
30 wherein the kit further comprises instructions for the detection, quantitation or characterization of the TAT protein transduction domain.

In another example, the present disclosure provides a kit for comprising at least one reagent specific for the detection of a level of a TAT protein transduction domain, wherein the detection reagent is a binding protein of the disclosure. In some examples, the TAT protein transduction domain is covalently linked to a cargo moiety. In some
5 examples, the kit further comprises instructions for the detection, quantitation or characterization of the TAT protein transduction domain.

In yet another aspect, the present disclosure provides an *in vitro* method of inhibiting the translocation of a TAT fusion molecule across a cell membrane, comprising contacting the TAT fusion molecule with an antigen binding protein as described herein, thereby inhibiting translocation of the TAT fusion molecule across the cell membrane.

5 In another example, the present disclosure provides a method of inhibiting the translocation of a TAT fusion molecule across a cell membrane, comprising contacting the TAT fusion molecule with an antigen binding protein of of the disclosure, thereby inhibiting translocation of the TAT fusion molecule across the cell membrane.

10 In yet another aspect, the present disclosure provides a use of an antigen binding protein as described herein in the manufacture of a medicament for inhibiting activity of HIV-TAT protein in a subject.

In another example, the present disclosure provides a method of inhibiting the activity of HIV-TAT protein in a subject, comprising administering to the subject an antigen binding protein of of the disclosure, thereby inhibiting activity of the HIV-TAT
15 protein in the subject.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 illustrates that polyclonal antibodies raised against the entire TAT-FXN fusion molecule recognize drug, but not in a TAT specific manner.

20 **Fig. 2** illustrates that polyclonal antibodies raised against KLH-TAT do not recognize mature frataxin, but do recognize BSA-TAT, showing specificity to the TAT epitope.

Fig. 3 is a bar graph showing relative peak area generated by a frataxin-derived tryptic peptide after immunopurification of an exemplary TAT frataxin fusion molecule using an anti-TAT rabbit polyclonal antibody (AC1058) and commercially available anti-frataxin antibodies (ab124680, ab113691 and ab110328) and a commercially available anti-TAT antibody (ab63957).
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Fig. 4A and Fig. 4B show the ability of nine of ten anti TAT antibodies of the invention to capture an exemplary TAT frataxin fusion molecule in a pharmacokinetic (PK) assay in human plasma.
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Fig. 5A shows that nine of ten anti TAT antibodies of the invention bind to an exemplary TAT frataxin fusion molecule in human plasma. **Fig. 5B** depicts the results of an anti-drug antibody (ADA) assay in human plasma, showing that the polyclonal anti-TAT antibody can function as a positive control in an ADA assay.

DETAILED DESCRIPTION OF THE INVENTION

This invention pertains to TAT peptide binding proteins, particularly anti-TAT peptide antibodies, or antigen-binding portions thereof, that bind to a TAT protein transduction domain, including TAT fusion molecules comprising a TAT protein
5 transduction domain, and uses thereof. Various aspects of the invention relate to

Claims

1. A binding protein comprising an antigen binding domain, said antigen binding domain comprising a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, wherein said binding protein is capable of binding a TAT protein transduction domain.
2. The binding protein of claim 1, wherein said antigen binding domain further comprises a heavy chain CDR2 domain comprising the amino acid sequence of SEQ ID NO: 3; and/or wherein said antigen binding domain further comprises a heavy chain CDR1 domain comprising the amino acid sequence of SEQ ID NO: 2; and/or wherein said antigen binding domain further comprises a light chain CDR3 domain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 8 and SEQ ID NO: 12; and/or wherein said antigen binding domain further comprises a light chain CDR2 domain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 7 and SEQ ID NO: 11; and/or wherein said antigen binding domain further comprises a light chain CDR1 domain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 10.
3. A binding protein comprising an antigen binding domain, said antigen binding domain comprising:

a heavy chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 3, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 2; and

a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 8, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 7, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 6; or a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 12, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 11, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 10,

wherein said binding protein is capable of binding a TAT protein transduction domain.

4. The binding protein of any one of claims 1-3, wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 14; and/or wherein said antigen binding domain comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 9, or SEQ ID NO: 13.

5. The binding protein of any one of claims 1-4, wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5; or wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 9; or wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 13; or wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 14 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 5.

6. A binding protein comprising an antigen binding domain, said antigen binding domain comprising a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 18, wherein said binding protein is capable of binding a TAT protein transduction domain.

7. The binding protein of claim 6, wherein said antigen binding domain further comprises a heavy chain CDR2 domain comprising the amino acid sequence of SEQ ID NO: 17; and/or wherein said antigen binding domain further comprises a heavy chain CDR1 domain comprising the amino acid sequence of SEQ ID NO: 16; and/or wherein said antigen binding domain further comprises a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 22; and/or wherein said antigen binding domain further comprises a light chain CDR2 domain comprising the amino acid sequence of SEQ ID NO: 21; and/or wherein said antigen binding domain further comprises a light chain CDR1 domain comprising the amino acid sequence of SEQ ID NO: 20.

8. A binding protein comprising an antigen binding domain, said antigen binding domain comprising:

a heavy chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 18, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 17, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 16; and

a light chain variable region comprising a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 22, a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 21, and a CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 20,

wherein said binding protein is capable of binding a TAT protein transduction domain.

9. The binding protein of any one of claims 6-8, wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 15; and/or wherein said antigen binding domain comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 19; and/or wherein said antigen binding domain comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 15 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 19.

10. The binding protein of any one of claims 1-9, wherein the TAT protein transduction domain comprises the amino acid sequence of SEQ ID NO: 23; optionally wherein the TAT protein transduction domain consists essentially of the amino acid sequence of SEQ ID NO: 23; and optionally wherein the TAT protein transduction domain is covalently linked to a cargo moiety; optionally:

(i) wherein the cargo moiety is a polypeptide; or (ii) wherein the cargo moiety is a frataxin polypeptide; or (iii) wherein the cargo moiety is an antibody; or (iv) wherein the cargo moiety is a nucleic acid, optionally wherein the nucleic acid is an siRNA, shRNA, miRNA, phosphorothioate modified RNA, aptamer, phosphorodiamidate morpholino oligomer (PMO), or

any combination thereof; or (v) wherein the cargo moiety is a small molecule, a liposome enclosing protein, a radionuclide or radionuclide labeled compound, or any combination thereof.

11. A binding protein comprising an antigen binding domain, wherein said binding protein is capable of binding to a TAT protein transduction domain that is covalently linked to a cargo moiety.

12. The binding protein of claim 11, wherein said antigen binding domain binds to an epitope comprising the amino acid residues of SEQ ID NO: 23; or wherein the cargo moiety is a polypeptide; or wherein the cargo moiety is a frataxin polypeptide; or wherein the cargo moiety is an antibody; or wherein the cargo moiety is a nucleic acid, optionally wherein the nucleic acid is an siRNA, shRNA, miRNA, phosphorothioate modified RNA, aptamer, phosphorodiamidate morpholino oligomer (PMO), or any combination thereof; or wherein the cargo moiety is a small molecule, a liposome enclosing protein, a radionuclide or radionuclide labeled compound, or any combination thereof.

13. The binding protein of any one of claims 1-12, wherein said binding protein is an antibody.

14. An antibody construct comprising the binding protein of any one of claims 1-13, said antibody construct further comprising a linker polypeptide or an immunoglobulin constant domain.

15. The antibody construct according to claim 14, wherein said binding protein is selected from the group consisting of: an immunoglobulin molecule, a monoclonal antibody, a murine antibody, a chimeric antibody, a CDR-grafted antibody, a humanized antibody, a single domain antibody, a Fv, a disulfide linked Fv, a scFv, a diabody, a Fab, a Fab', a F(ab')₂, a multispecific antibody, a dual specific antibody, and a bispecific antibody; and/or wherein said binding protein comprises a heavy chain immunoglobulin constant domain selected from the group consisting of: a IgM constant domain, a IgG₄ constant domain, a IgG₁ constant domain, a IgE constant domain, a IgG₂ constant domain, a IgG₃ constant domain and a IgA constant domain; optionally wherein said binding protein comprises a IgG₁ constant domain or wherein said heavy chain immunoglobulin constant domain is not IgM.

16. An isolated nucleic acid encoding a binding protein amino acid sequence of any one of claims 1-13 or an antibody construct amino acid sequence of claim 14 or 15.
17. A vector comprising an isolated nucleic acid according to claim 16; optionally wherein said vector is selected from the group consisting of pcDNA, pTT, pTT3, pEFBOS, pBV, pJV, pBJ, pGEX, VSV, pBR322, pCMV-HA, pEN, YAC, BAC, Bacteriophage Lamda, Phagemid, pCAS9, pCEN6, pYES1L, p3HPRT1, pFN2A, pBC, pTZ, pGEM, pGEMK, pEX, pSAR, pCEP, Cosmids, pBluescript, pKJK, pFloxin, pCP, pHR, pUC, and pMAL.
18. A host cell comprising a vector according to claim 17; optionally wherein said host cell is a prokaryotic cell or a eukaryotic cell, or wherein said host cell is selected from the group consisting of a CHO cell, a COS cell, a yeast cell, an insect Sf9 cell, HEK-293 cell, ExpiCHO cell, Expi-293f cell, and *E.Coli* cell; further optionally: (a) wherein said prokaryotic host cell is *E. Coli*; or (b) wherein said eukaryotic host cell is selected from the group consisting of a protist cell, an insect cell, an animal cell, a plant cell and a fungal cell, further optionally wherein said animal cell is a mammalian cell or an avian cell; or (c) wherein said yeast cell is *Saccharomyces cerevisiae*.
19. A method of producing an antibody, or antigen binding portion thereof, comprising culturing the host cell of claim 18 in a culture medium so that said isolated nucleic acid is expressed and said antibody is produced.
20. An antibody produced according to the method of claim 19.
21. A transgenic mouse comprising the host cell of claim 18, wherein the mouse expresses a polypeptide encoded by the nucleic acid, or an antigen binding portion thereof, that binds to a TAT protein transduction domain.
22. A hybridoma that produces the antibody construct of claim 14 or 15.
23. The binding protein of any one of claims 1-13, which is immobilized on a solid support or which is conjugated to a detection molecule; optionally:
- (a) wherein the solid support is a plate, a bead, or a chromatography resin, further optionally wherein the bead or chromatography resin comprises protein A agarose or protein G agarose; or

(b) wherein the detection molecule is horseradish peroxidase, sulfotag, alkaline phosphatase, cresol violet, quantum dots, FITC, an infrared molecule, a radiolabel, or an EPR spin tracer label.

24. A method for detecting and/or quantifying the level of a TAT fusion molecule in a sample, comprising contacting the sample with the binding protein of any one of claims 1-13 under conditions such that the binding protein binds to TAT protein transduction domain in the sample, to thereby detect and/or quantify the level of the TAT fusion molecule in the sample.

25. The method of claim 24, wherein the sample is a biological sample, optionally wherein the biological sample is a liquid sample or a tissue sample; or wherein the TAT fusion molecule comprises a TAT protein transduction domain covalently linked to a cargo moiety; optionally (i) wherein the cargo moiety is a polypeptide; or (ii) wherein the cargo moiety is a frataxin polypeptide; or (iii) wherein the cargo moiety is an antibody; or (iv) wherein the cargo moiety is a nucleic acid, optionally wherein the nucleic acid is an siRNA, shRNA, miRNA, phosphorothioate modified RNA, aptamer, phosphorodiamidate morpholino oligomer (PMO), or any combination thereof; or (v) wherein the cargo moiety is a small molecule, a liposome enclosing protein, a radionuclide or radionuclide labeled compound, or any combination thereof.

26. The method of claim 24, further comprising assessing the stability of the TAT fusion molecule.

27. A method of isolating and/or purifying a TAT fusion molecule present in a mixture, wherein said TAT fusion molecule comprises a TAT protein transduction domain covalently linked to a cargo moiety, comprising (a) contacting said mixture comprising the TAT fusion molecule with the immobilized binding protein of claim 23 under conditions such that the TAT fusion molecule binds to the immobilized binding protein; (b) eluting said TAT fusion molecule from the immobilized binding protein.

28. A kit comprising at least one reagent specific for the detection of a level of a TAT protein transduction domain, wherein the detection reagent is a binding protein of any one of claims 1-13, optionally: wherein the TAT protein transduction domain is covalently linked to a cargo moiety and/or wherein the kit further comprises instructions for the detection, quantitation or characterization of the TAT protein transduction domain.

29. An *in vitro* method of inhibiting the translocation of a TAT fusion molecule across a cell membrane, comprising contacting the TAT fusion molecule with an antigen binding protein of any one of claims 1-13, thereby inhibiting translocation of the TAT fusion molecule across the cell membrane.

30. Use of an antigen binding protein of any one of claims 1-13 in the manufacture of a medicament for inhibiting activity of HIV-TAT protein in a subject.