

section below. As described in the Examples section below, anti-PNAd antibody MHA112 displays improved binding affinity to cells expressing PNAd (Example 6) and improved ability to block T cell homing to lymph nodes (Example 4).

Administration of drug conjugated to MHA112 resulted in reduced tumor growth, reduced tumor metastasis, and reduced tumor-draining lymph node fibrosis (Example 7), in addition to increased survival time (Example 8). Moreover, administration of drug conjugated to MHA112 also increased survival time in pancreas tumor model (Example 9).

The antibodies and antigen-binding fragments thereof may be characterized by comprising in their variable region, e.g., binding domain, at least one complementarity determining region (CDR) of the VH and/or VL variable region comprising any one of the amino acid sequences depicted in **FIG. 5**. The corresponding nucleotide sequences encoding the above-identified variable regions are set forth in Table 4 below. An exemplary set of CDRs of the above amino acid sequences of the VH and/or VL region is depicted in **FIG. 5** and Table 2. The corresponding framework regions for the CDRs of Table 2 are shown in Table 3. However, as discussed in the following the person skilled in the art is well aware of the fact that in addition or alternatively CDRs may be used, which differ in their amino acid sequence from those set forth in **FIG. 5** by one, two, three or even more amino acids in case of CDR2 and CDR3.

Table 2: IMGT CDR Sequences.

	CDR1	CDR2	CDR3
Heavy Chain	GFSLTSY (SEQ ID NO: 3)	WGGGS (SEQ ID NO: 4)	HSKGGYFDV (SEQ ID NO: 5)
Light Chain	SASSSVSYMH (SEQ ID NO: 8)	EISKLAS (SEQ ID NO: 9)	QQWNYPLIT (SEQ ID NO: 10)

Table 3: Framework Region Sequences

	FR1	FR2	FR3	FR4
Heavy Chain	QVQLKESGPGL VAPSQSLTCT VS (SEQ ID NO:11)	GVDWVRQPPG KGLEWLGVI (SEQ ID NO:12)	TNYNSALMSRL SISKDNSKSQVF LKMNSLQTDDT AMYCAK (SEQ ID NO:13)	WGTGTTVTVSS (SEQ ID NO:14)
Light Chain	EIVLTQSPAITA ASLGQKVTITC (SEQ ID NO:15)	WYQQKSGTSPK PWIY (SEQ ID NO:16)	GVPARFSGSGS GTSYSLTISSME AEDAAIYYC (SEQ ID NO:17)	FGAGTKLELK (SEQ ID NO:18)

Table 4: Variable Region Sequences

	Nucleotide	Amino Acid
Heavy Chain	CAGGTGCAGCTGAAGGAGTCAGGACCTGG CCTGGTGGCGCCCTCACAGAGCCTGTCCAT CACTTGCACTGTCTCTGGGTTTTTCATTAAC CAGCTATGGTGTAGACTGGGTTCGCCAGCC TCCAGGAAAGGGTCTGGAGTGGCTGGGAG TAATATGGGGTGGTGGGAAGCACAAATTAT AATTCAGCTCTCATGTCCAGACTGAGCATC AGCAAAGACAACCTCCAAGAGCCAAGTTTT CTTAAAAATGAACAGTCTGCAAACCTGATG ACACAGCCATGTACTACTGTGCCAAACAT AGTAAAGGGGGGTACTTCGATGTCTGGGG CACAGGGACCACGGTCACCGTCTCCTCA (SEQ ID NO: 1)	QVQLKESGPGL VAPSQSLSITCT VSGFSLTSYGV DWVRQPPGKGL EWLGVIWGGGS TNYNSALMSRL SISKDNSKSQVF LKMNSLQTDDT AMYYCAKHSK GGYFDVWGTG TTVTVSS (SEQ ID NO: 2)
Light Chain	GAAATTGTGCTCACTCAGTCTCCAGCCATC ACAGCTGCATCTCTGGGGCAAAGGTCAC CATCACCTGCAGTGCCAGCTCAAGTGTA GTTACATGCACTGGTACCAGCAGAAGTCA GGCACCTCCCCCAAACCATGGATTTATGAA ATATCCAAACTGGCTTCTGGAGTCCCAGCT CGCTTCAGTGGCAGTGGGTCTGGGACCTCT TACTCTCTCACAATCAGCAGCATGGAGGCT GAAGATGCTGCCATTTATTACTGCCAGCAG TGGAATTATCCTCTTATCACGTTCCGGTGCT GGGACCAAGCTGGAGCTGAAA (SEQ ID NO: 6)	EIVLTQSPAITA ASLGQKVTITCS ASSSVSYMHWY QKSGTSPKPWI YEISKLASGVPA RFSGSGSGTSYS LTISSMEAEDAA IYYCQQWNYPL ITFGAGTKLELK (SEQ ID NO: 7)

In some embodiments, an antibody or antigen-binding fragment thereof described herein comprises at least one CDR comprising, or consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5 and 8-10. In some embodiments, an antibody or antigen-binding fragment thereof described herein comprises one, two, three, four, five or six CDRs comprising, or consisting of an amino acid sequence selected from the group consisting of SEQ ID NO: 3-5 and 8-10 (see, e.g., Table 2).

In some embodiments, the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5. In some embodiments, the antibody or PNA-binding fragment thereof comprises a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ

WHAT IS CLAIMED IS:

1. An anti-peripheral lymph node addressin (PNAd) antibody, or a PNAd-binding fragment thereof, comprising:
 - (a) a heavy chain variable region (VH), wherein the VH comprises a VH complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; and
 - (b) a light chain variable region (VL), wherein the VL comprises a VL CDR1 comprising the amino acid sequence of SEQ ID NO:8, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:9, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:10.
2. The antibody, or PNAd-binding fragment thereof, of claim 1, wherein the VH comprises a VH framework region 1 (FR1) comprising the amino acid sequence set forth in SEQ ID NO:11, a VH FR2 comprising the amino acid sequence set forth in SEQ ID NO:12, a VH FR3 comprising the amino acid sequence set forth in SEQ ID NO:13, and a VH FR4 comprising the amino acid sequence set forth in SEQ ID NO:14, and/or the VL comprises a VL FR1 comprising the amino acid sequence set forth in SEQ ID NO:15, a VL FR2 comprising the amino acid sequence set forth in SEQ ID NO:16, a VL FR3 comprising the amino acid sequence set forth in SEQ ID NO:17, and a VL FR4 comprising the amino acid sequence set forth in SEQ ID NO:18.
3. The antibody, or PNAd-binding fragment thereof of claim 1 or 2, wherein:
 - (a) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:2;
 - (b) the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:7;
 - (c) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:2 and the VL has at least 80% sequence identity to the amino acid sequence

of SEQ ID NO:7;

(d) the VH comprises the amino acid sequence of SEQ ID NO:2; or

(e) the VL comprises the amino acid sequence of SEQ ID NO:7.

4. An anti-PNAd antibody, or a PNAd-binding fragment thereof, comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:2 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:7.

5. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 3, which is an antibody selected from the group consisting of a murine antibody, a chimeric antibody, and a humanized antibody.

6. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 4, which comprises an antibody.

7. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 4, which is an antibody, wherein the antibody comprises human-derived heavy chain and light chain constant regions.

8. The antibody, or PNAd-binding fragment thereof, of claim 6 or 7, wherein the antibody comprises a heavy chain constant region of isotype immunoglobulin mu (IgM).

9. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 4, which comprises a PNAd-binding fragment of the antibody, wherein the PNAd-binding fragment is selected from the group consisting of a single chain Fv fragment (scFv), an F(ab') fragment, an F(ab) fragment, and an F(ab')₂ fragment.

10. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 4, which is a diabody.
11. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 10, comprising an agent conjugated to the antibody or PNAd-binding fragment thereof.
12. The antibody, or PNAd-binding fragment thereof, of claim 11, wherein
the conjugation is covalent conjugation; or
the conjugation is via a linker, optionally, wherein the linker is polyethylene glycol.
13. The antibody, or PNAd-binding fragment thereof, of claim 11 or 12, wherein the agent is an imaging agent, a cytotoxic agent, or a drug.
14. The antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 10, comprising a drug-containing polymeric particle conjugated to the antibody or PNAd-binding fragment thereof.
15. The antibody, or PNAd-binding fragment thereof, of claim 13 or 14, wherein the drug is an immunosuppressive or immunoregulatory drug.
16. The antibody, or PNAd-binding fragment thereof, of claim 13 or 14, wherein the drug is Taxol, Tacrolimus, mycophenolate, mofetil, cyclosporine, sirolimus, fingolimod, myriocin, cyclophosphamide, a corticosteroid, rapamycin, mycophenolate, mofetil, a checkpoint inhibitor, an anti-inflammatory agent, a chemotherapeutic agent, an anti-CD3 antibody, an anti-CD25 antibody, an anti-IL6

antibody, an anti-CDLA-4 antibody, adalimumab, an anti-CD52 antibody, an antimetabolite, an alkylating agent, an anthracycline, an antibiotic, or an antimitotic agent

17. A polynucleotide comprising:

(i) nucleic acid sequences encoding the antibody, or PNAd-binding fragment thereof, of any one of claims 1 to 10, or

(ii) nucleic acid sequences encoding a VH, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:2, or

(iii) nucleic acid sequences encoding a heavy chain, wherein the heavy chain comprises a VH, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:2, or

(iv) nucleic acid sequences encoding a VL, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:7, or

(v) nucleic acid sequences encoding a light chain, wherein the light chain comprises a VL, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:7.

18. The polynucleotide of claim 17, comprising:

(a) the nucleic acid sequences in (ii) or (iii), wherein the nucleic acid sequences comprise the nucleic acid sequence set forth in SEQ ID NO:1; and/or

(b) nucleic acid sequences in (iv) or (v), wherein the nucleic acid sequences comprise the nucleic acid sequence set forth in SEQ ID NO:6.

19. A vector comprising:

(i) the polynucleotide of claim 17, part (ii) or claim 17, part (iv) operably linked to a promoter or

(ii) the polynucleotide of claim 17, part (iii) operably linked to a promoter,

or

(iii) the polynucleotide of claim 17, part (v) operably linked to a promoter,

or

(iv) the polynucleotide of claim 17, part (iii) operably linked to a first promoter and the polynucleotide of claim 17, part (v) operably linked to a second promoter.

20. A host cell comprising:

(i) the polynucleotide of claim 17, part (ii) or claim 17, part (iv) , wherein the polynucleotide is operably linked to a promoter, or

(ii) the polynucleotides of claim 17, part (iii) and claim 17, part (v) , wherein each polynucleotide is operably linked to a promoter, or

(iii) the vector of claim 19, part (i), or

(iv) the vector of claim 19, part (ii) and the vector of claim 19, part (iii), or

(v) the vector of claim 19, part (iv).

21. A method of producing an anti-peripheral lymph node addressin (PNAd) antibody or PNAd-binding fragment thereof, comprising:

(a) culturing the host cell of claim 20, part (ii), claim 20, part (iv) or claim 20, part (v); and

(b) isolating the antibody or PNAd-binding fragment thereof from the culture.

22. A pharmaceutical composition comprising (i) a therapeutically effective amount of the antibody or PNAd-binding fragment thereof of any one of claims 1 to 16 and a pharmaceutically acceptable carrier.

23. The pharmaceutical composition of claim 22 for use in therapy.

24. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for suppressing a lymphocyte-mediated immune response in a subject in need thereof.
25. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for diagnosing, treating, or delaying progression an autoimmune disorder in a subject in need thereof.
26. The use of claim 25, wherein the autoimmune disorder is type 1 diabetes or rheumatoid arthritis.
27. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for treating lymphocyte-mediated inflammation in a subject in need thereof.
28. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for diagnosing, treating or reducing metastasis of a PNAd-expressing malignancy in a subject in need thereof.
29. The use of claim 28, wherein the PNAd-expressing malignancy is lymphoma, breast cancer, or pancreatic cancer.
30. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for delivering a diagnostic or a therapeutic agent to a subject in need thereof, optionally wherein the diagnostic agent or therapeutic agent is delivered to one or more lymphoid tissues or one or more sites of chronic inflammation in the subject.

31. The use of any one of claims 24 to 30, wherein the antibody, or PNAd-binding fragment thereof, is conjugated to a diagnostic agent or a therapeutic agent.

32. The use of any one of claims 24 to 30, wherein the antibody, or PNAd-binding fragment thereof, is conjugated to a therapeutic agent, wherein the therapeutic agent is taxol, Tacrolimus, mycophenolate, mofetil, cyclosporine, sirolimus, fingolimod, myriocin, cyclophosphamide, a corticosteroid, rapamycin, mycophenolate, mofetil, a checkpoint inhibitor, an anti-inflammatory agent, a chemotherapeutic agent, an anti-CD3 antibody, an anti-CD25 antibody, an anti-IL6 antibody, an anti-CDLA-4 antibody, adalimumab, an anti-CD52 antibody, an antimetabolite, an alkylating agent, an anthracycline, an antibiotic, or an antimitotic agent.

33. The use of any one of claims 24 to 30, wherein the medicament comprises a drug-containing polymeric particle conjugated to the antibody or PNAd-binding fragment thereof, optionally, wherein the medicament is to be delivered to one or more lymphoid tissues, or one or more sites of chronic inflammation in the subject.

34. The use of claim 33, wherein the drug comprises taxol, Tacrolimus, mycophenolate, mofetil, cyclosporine, sirolimus, fingolimod, myriocin, cyclophosphamide, a corticosteroid, rapamycin, mycophenolate, mofetil, a checkpoint inhibitor, an anti-inflammatory agent, a chemotherapeutic agent, an anti-CD3 antibody, an anti-CD25 antibody, an anti-IL6 antibody, an anti-CDLA-4 antibody, adalimumab, an anti-CD52 antibody, an antimetabolite, an alkylating agent, an anthracycline, an antibiotic, or an antimitotic agent.

35. The use of any one of claims 24 to 34, wherein the subject is a human.