

The structure of PACAP is well-known in the art (see, for example, A. Miyata, A. et al., Biochem Biophys Res Commun 170: 643-648 (1990)) as are anti-PACAP antibodies. For example, U.S. Patent No. 5,486,472A, International Patent Application Publication No. WO/2012/106407 A3, and U.S. Patent Application Publication No. 2016-304604 all disclose various anti-PACAP antibodies and potential uses thereof. However, to date, no antibody targeting PACAP has been approved for therapeutic use. Thus, there remains a need for alternative anti-PACAP antibodies. In particular, there remains a need for alternative anti-PACAP antibodies that neutralize PACAP with high potency, provide a sustained duration of action, and are capable of treating pain including primary and secondary headaches and migraines including chronic migraine. As with all therapeutic treatments, safety and toxicity remain a limitation and alternative anti-PACAP antibodies must not be attendant on unacceptable immunogenicity. There, thus, remains a need for alternative anti-PACAP antibodies which present a reduced risk of immunogenicity in humans. Such anti-PACAP antibodies will preferably also possess good physical-chemical properties to facilitate development, manufacturing, and formulation.

Summary

In one aspect, the present disclosure refers to an antibody that binds human pituitary adenylate cyclase-activating peptide comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises complementarity determining regions (CDRs) HCDR1, HCDR2, and HCDR3 and the LCVR comprises CDRs LCDR1, LCDR2, and LCDR3, wherein the amino acid sequence of HCDR1 is SEQ ID NO.3, the amino acid sequence of HCDR2 is SEQ ID NO.4, the amino acid sequence of HCDR3 is SEQ ID NO.5, the amino acid sequence of LCDR1 is SEQ ID NO.6, the amino acid sequence of LCDR2 is SEQ ID NO.7, and the amino acid sequence of LCDR3 is SEQ ID NO.8.

In another aspect, the present disclosure refers to an antibody that binds human pituitary adenylate cyclase-activating peptide comprising a heavy chain (HC) and a light chain (LC), wherein the amino acid sequence of the HC is SEQ ID NO.1 and the amino acid sequence of the LC is SEQ ID NO.2.

In yet another aspect, the present disclosure refers to an antibody disclosed herein, for use in therapy.

In a further aspect, the present disclosure refers to an antibody disclosed herein, for use in the treatment of one of primary headache, secondary headache and migraine.

In another aspect, the present disclosure refers to an antibody disclosed herein, for use in the treatment of a trigeminal autonomic cephalalgias.

In yet another aspect, the present disclosure refers to a use of an antibody disclosed herein, in the manufacture of a medicament for the treatment of one of primary headache, secondary headache and migraine.

In a further aspect, the present disclosure refers to a use of an antibody disclosed herein, in the manufacture of a medicament for the treatment of a trigeminal autonomic cephalalgias.

Description

The present invention provides an antibody that binds human PACAP and which comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises the complementarity determining regions (CDRs) HCDR1, HCDR2 and HCDR3 and the LCVR comprises CDRs LCDR1, LCDR2 and LCDR3, wherein the amino acid sequence of HCDR1 is SEQ ID NO.3, the amino acid sequence of HCDR2 is SEQ ID NO.4, the amino acid sequence of HCDR3 is SEQ ID NO.5, the amino acid sequence of LCDR1 is SEQ ID NO.6, the amino acid sequence of LCDR2 is SEQ ID NO.7, and the amino acid sequence of LCDR3 is SEQ ID NO.8. In a particular embodiment HCDR2 comprises aspartic acid at residue 13, HCDR3 comprises asparagine at residue 8, LCDR1 comprises serine at residue 7, and LCDR2 comprises leucine at residue 7. In another particular embodiment, HCDR2 comprises alanine at residue 13, HCDR3 comprises threonine at residue 8, LCDR1 comprises tryptophan at residue 7, and LCDR2 comprises phenylalanine at residue 7. In a further particular embodiment, HCDR2 comprises glutamic acid at residue 13, HCDR3 comprises threonine at residue 8, LCDR1 comprises tryptophan at residue 7, and LCDR2 comprises phenylalanine at residue 7. In an even further particular embodiment, HCDR2 comprises

WE CLAIM:

1. An antibody that binds human pituitary adenylate cyclase-activating peptide comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises complementarity determining regions (CDRs) HCDR1, HCDR2, and HCDR3 and the LCVR comprises CDRs LCDR1, LCDR2, and LCDR3, wherein the amino acid sequence of HCDR1 is SEQ ID NO.3, the amino acid sequence of HCDR2 is SEQ ID NO.4, the amino acid sequence of HCDR3 is SEQ ID NO.5, the amino acid sequence of LCDR1 is SEQ ID NO.6, the amino acid sequence of LCDR2 is SEQ ID NO.7, and the amino acid sequence of LCDR3 is SEQ ID NO.8.
2. The antibody of Claim 1, wherein HCDR2 comprises aspartic acid at residue 13; HCDR3 comprises asparagine at residue 8; LCDR1 comprises serine at residue 7; and LCDR2 comprises leucine at residue 7.
3. The antibody of Claim 1, wherein HCDR2 comprises alanine at residue 13; HCDR3 comprises threonine at residue 8; LCDR1 comprises tryptophan at residue 7; and LCDR2 comprises phenylalanine at residue 7.
4. The antibody of Claim 1, wherein HCDR2 comprises glutamic acid at residue 13; HCDR3 comprises threonine at residue 8; LCDR1 comprises tryptophan at residue 7; and LCDR2 comprises phenylalanine at residue 7.
5. The antibody of Claim 1, wherein HCDR2 comprises glutamine at residue 13; HCDR3 comprises threonine at residue 8; LCDR1 comprises tryptophan at residue 7; and LCDR2 comprises phenylalanine at residue 7.
6. The antibody of Claim 1, comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the amino acid sequence of the HCVR is SEQ ID NO.9 and the amino acid sequence of the LCVR is SEQ ID NO. 10.

7. The antibody of Claim 6, wherein HCVR comprises aspartic acid at residue 62 and asparagine at residue 104, and wherein LCVR comprises serine at residue 30 and leucine at residue 55.
8. The antibody of Claim 6, wherein HCVR comprises alanine at residue 62 and threonine at residue 104, and wherein LCVR comprises tryptophan at residue 30 and phenylalanine at residue 55.
9. The antibody of Claim 6, wherein HCVR comprises glutamic acid at residue 62 and threonine at residue 104, and wherein LCVR comprises tryptophan at residue 30 and phenylalanine at residue 55.
- 10 The antibody of Claim 6, wherein HCVR comprises glutamine at residue 62 and threonine at residue 104, and wherein LCVR comprises tryptophan at residue 30 and phenylalanine at residue 55.
11. An antibody that binds human pituitary adenylate cyclase-activating peptide comprising a heavy chain (HC) and a light chain (LC), wherein the amino acid sequence of the HC is SEQ ID NO.1 and the amino acid sequence of the LC is SEQ ID NO.2.
12. The antibody of Claim 11, wherein HC comprises aspartic acid at residue 62, asparagine at residue 104, proline at residue 231, alanine at residue 237 and alanine at residue 238, and wherein LC comprises serine at residue 30 and leucine at residue 55.
13. The antibody of Claim 11, wherein HC comprises alanine at residue 62, threonine at residue 104, proline at residue 231, alanine at residue 237 and alanine at residue 238, and wherein LC comprises tryptophan at residue 30 and phenylalanine at residue 55.
14. The antibody of Claim 11, wherein HC comprises glutamic acid at residue 62, threonine at residue 104, proline at residue 231, alanine at residue 237 and alanine at

residue 238, and wherein LC comprises tryptophan at residue 30 and phenylalanine at residue 55.

15. The antibody of Claim 11, wherein HC comprises glutamine at residue 62, threonine at residue 104, proline at residue 231, alanine at residue 237 and alanine at residue 238, and wherein LC comprises tryptophan at residue 30 and phenylalanine at residue 55.

16. An antibody of any one of Claims 1-15, for use in therapy.
17. An antibody of any one of Claims 1-15, for use in the treatment of one of primary headache, secondary headache and migraine.
18. An antibody of any one of Claims 1-15, for use in the treatment of a trigeminal autonomic cephalalgias.
19. The antibody of Claim 18, wherein the trigeminal autonomic cephalalgias is one of episodic cluster headache, chronic cluster headache, paroxysmal hemicranias and unilateral neuralgiform headache attack.
20. Use of an antibody of any one of Claims 1-15 in the manufacture of a medicament for the treatment of one of primary headache, secondary headache and migraine.
21. Use of an antibody of any one of Claims 1-15 in the manufacture of a medicament for the treatment of a trigeminal autonomic cephalalgias.
22. The use of Claim 21, wherein the trigeminal autonomic cephalalgias is one of episodic cluster headache, chronic cluster headache, paroxysmal hemicranias and unilateral neuralgiform headache attack.