Claims

1) An isolated fusion protein comprising a peptide antagonist of Kv1.3 conjugated to a half-life extending moiety, wherein the peptide antagonist of Kv1.3 comprises the amino acid sequence $GVPXaa_1Xaa_2VKCXaa_3ISRQCXaa_4Xaa_5PCKDAGMRFGKCMNGKCHCTPK$ (SEQ ID NO: 427); wherein

a) Xaa_1 is I or T;

b) Xaa_2 is N or D;

c) Xaa_3 is K or R;

d) Xaa_4 is I or E; and

e) Xaa_5 is E or K, and has an IC_{50} value of about $1x10^{-8}$ M or less towards Kv1.3 in a whole cell patch clamp assay on Chinese hamster ovary (CHO) cells transfected with Kv1.3, and is at least l00-fold more selective towards Kv1.3 when compared to a fusion protein comprising a wild—type Odk2 peptide of SEQ ID NO: 1 conjugated to the half—life extending moiety , when selectivity is calculated as a ratio of Kv1.1 IC_{50} value to Kv1.3 IC_{50} value in the whole cell patch clamp assay on CHO cells transfected with Kv1.3 or Kv1.1.

2) The fusion protein of claim 1, wherein the peptide antagonist of Kv1.3 comprises the amino acid sequence of SEQ ID NOs: 3, 22, 34 or 42.

3) The fusion protein of claim 2, wherein the half—life extending moiety is human serum albumin (HSA), albumin binding domain (ADB), or polyethylene glycol (PEG).

4) The fusion protein of claim 3, wherein the half—life extending moiety is human serum albumin.

5) The fusion protein of claim 3, wherein the half—life extending moiety is conjugated to the peptide antagonist of Kv1.3 via a linker.

6) The fusion protein of claim 5, wherein the linker comprises the amino sequence of SEQ ID NOs: 112—122 or 428.

7) The fusion protein of claim 6, wherein
a) the peptide antagonist of Kv1.3 comprises the amino acid sequence of SEQ ID NOs: 3, 22, 34 or 42;
b) the linker comprises the amino acid sequence of SEQ ID NO: 116 or SEQ ID NO:119; and
c) the half—life extending moiety is human serum albumin.

8) The fusion protein of claim 6, wherein
a)the peptide antagonist of Kv1.3 comprises the amino acid sequence of SEQ ID NO: 42;
b)the linker comprises the amino acid sequence of SEQ ID NO: 116; and
c)the half-life extending moiety is human serum albumin.

9) The fusion protein of claim 6, wherein
a)the peptide antagonist of Kv1.3 comprises the amino acid sequence of SEQ ID NO: 42;
b)the C-terminal extension comprises the amino acid sequence of SEQ ID NO: 209;
c)the linker comprises the amino acid sequence of SEQ ID NO: 116; and
d)the half-life extending moiety is human serum albumin.

10) A pharmaceutical composition comprising the fusion protein of claim 2 and a pharmaceutically acceptable carrier.

11) An isolated peptide antagonist of Kv1.3 comprising the amino acid sequence GVPXaa$_1$Xaa$_2$VKCXaa$_3$ISRQCXaa$_4$Xaa$_5$PCKDAGMRFGKCMNGKCHCTPK (SEQ ID NO: 427);

wherein

a)Xaa$_1$ is I or T;

b)Xaa$_2$ is N or D;

c)Xaa$_3$ is K or R;

d)Xaa$_4$ is I or E; and

e)Xaa$_5$ is E or K, wherein the peptide antagonist of Kv1.3 has an IC$_{50}$ value of about 1x10^{-8} M or less towards Kv1.3 in a whole cell patch clamp assay on Chinese hamster ovary (CHO) cells transfected with Kv1.3, and is at least 100-fold more selective towards Kv1.3 when compared to a fusion protein comprising a wild-type Odk2 peptide of SEQ ID NO: 1 conjugated to the half-life extending moiety , when selectivity is calculated as a ratio of Kv1.1 IC$_{50}$ value to Kv1.3 IC$_{50}$ value in the whole cell patch clamp assay on CHO cells transfected with Kv1.3 or Kv1.1.

12) The peptide antagonist of Kv1.3 of claim 11, comprising the amino acid sequence of SEQ ID NOs: 3 or 42.