

**(12) STANDARD PATENT**  
**(19) AUSTRALIAN PATENT OFFICE**

(11) Application No. **AU 2015254558 B2**

(54) Title  
**Ion channel modulators and uses thereof**

(51) International Patent Classification(s)  
**C07K 16/28** (2006.01)

(21) Application No: **2015254558**

(22) Date of Filing: **2015.05.02**

(87) WIPO No: **WO15/166105**

(30) Priority Data

(31) Number  
**61/987,929**

(32) Date  
**2014.05.02**

(33) Country  
**US**

(43) Publication Date: **2015.11.05**

(44) Accepted Journal Date: **2021.02.25**

(71) Applicant(s)  
**MedImmune Limited**

(72) Inventor(s)  
**Williams, Wendy A.; Jones, Clare; Button, James; Linley, John; Huang, Ling; Snijder, Harm Jan; Shibata, Yoko; Sridharan, Sudharsan; Groves, Maria; Dobson, Claire**

(74) Agent / Attorney  
**Phillips Ormonde Fitzpatrick, PO Box 323, COLLINS STREET WEST, VIC, 8007, AU**

(56) Related Art  
**Makoto Tsuda et al., "P2X4 receptors induced in spinal microglia gate tactile allodynia after nerve injury", NATURE, (2003), Vol.424, doi:doi:10.1038/nature01786, pages 778 - 783**  
**US 20050074819 A1**  
**US 20080287467 A1**  
**US 6242216 B1**  
**Rebecca J.Gum et al., "P2X receptor antagonists for pain management: examination of binding and physicochemical properties", Purinergic Signalling, (2012), Vol.8, Suppl.1, pages 41 - 56**



(43) International Publication Date  
5 November 2015 (05.11.2015)

(10) International Publication Number  
**WO 2015/166105 A3**

(51) International Patent Classification:  
C07K 16/28 (2006.01)

(21) International Application Number:  
PCT/EP2015/059633

(22) International Filing Date:  
2 May 2015 (02.05.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
61/987,929 2 May 2014 (02.05.2014) US

(71) Applicant: **MEDIMMUNE LIMITED** [GB/GB]; Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB).

(72) Inventors: **WILLIAMS, Wendy A**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **JONES, Clare**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **BUTTON, James**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **LINLEY, John**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **HUANG, Ling**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **SNIJDER, Harm Jan**; c/o AstraZeneca, R&D Molndal, -431 83 Molndal (SE). **SHIBATA, Yoko**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **SRIDHARAN, Sudharsan**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **GROVES, Maria**; c/o MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB). **DOBSON, Claire**; c/o MedImmune

Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB).

(74) Agent: **WINTER, Christopher Spencer**; MedImmune Limited, Milstein Building, Granta Park, Cambridge, Cambridgeshire CB21 6GH (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:  
30 December 2015

(54) Title: ION CHANNEL MODULATORS AND USES THEREOF

(57) Abstract: The invention provides antibodies that specifically bind a P2X4 polypeptide and modulate P2X4 channel activity, recombinant P2X4 polypeptides and methods for generating such polypeptides, as well as compositions and methods for generating anti-P2X4 antibodies, and methods of using P2X4 antibodies for the treatment of neuropathic pain and other indications.



WO 2015/166105 A3

## ION CHANNEL MODULATORS & USES THEREOF

### BACKGROUND OF THE INVENTION

Chronic pain serves no beneficial purpose, but arises from pathological alterations in nociceptive neural networks. Neuropathic pain is a form of chronic pain that arises after nerve injury caused by trauma, infection, or pathology. Neuropathic pain persists long after the initiating event has healed. While neurons are involved in neuropathic pain, they are unlikely to be the sole cell type mediating this condition. There is a growing body of evidence that supports a role for glia–neuron interactions in establishing and maintaining neuropathic pain. Microglia, in particular, have emerged as key players in neuropathic pain. The microglial P2X4 receptor appears to be important in the development and maintenance of neuropathic pain.

The ion channel P2X4 is one of seven members of a family of purinergic, cation permeable channels. Each P2X4 subunit has two transmembrane domains, separated by a large ~280 amino acid extracellular domain. Functional channels are formed of a trimeric arrangement of subunits with a central pore. The P2X4 channel is activated by binding of the ligand adenosine 5'-triphosphate (ATP) to residues contained within its extracellular domain. Activation of these receptors instigates a series of conformational changes that allow cations, such as  $\text{Ca}^{2+}$  and  $\text{Na}^{+}$ , entry into the cell through a cation selective channel. P2X4 activation and upregulation is thought to be a key driver of neuropathic pain. Downstream of P2X4 activation, microglia release brain derived neurotrophic factor (BDNF), which acts on spinal lamina I neurons to reduce expression of a neuronal chloride transporter KCC2, thereby altering the electrochemical gradient for chloride and rendering one of the main inhibitory neurotransmitters GABA excitatory. Therefore, P2X4-mediated BDNF release in spinal cord is thought to be a key driver of neuropathic pain.

Neuropathic pain fails to respond to currently available analgesics, and is considered to be one of the most debilitating chronic pain conditions. Accordingly, improved methods for treating neuropathic pain, particularly pain mediated by P2X4 are urgently required.

### SUMMARY OF THE INVENTION

As described below, the present invention provides antibodies that specifically bind a P2X4 polypeptide and modulate P2X4 channel activity, recombinant P2X4 polypeptides and

methods for generating such polypeptides, as well as compositions and methods for generating anti-P2X4 antibodies, and methods of using P2X4 antibodies for the treatment of neuropathic pain and other indications.

In a first aspect, the invention provides an antibody or antigen binding fragment thereof that specifically binds a human P2X4 polypeptide and modulates channel activity. In one embodiment, the antibody is a P2X4 potentiator. In another embodiment, the antibody is a P2X4 antagonist. In another embodiment, the antibody is a P2X4 modulator. In another embodiment, the antibody is a P2X4 antagonist that reduces P2X4 biological activity by at least about 10, 25, 50, 75, 85, 90 or 95%. In another embodiment, the antibody binds an epitope containing human P2X4 amino acids 110 -166. In another embodiment, the antibody binds an epitope containing one or more human P2X4 amino acids selected from any one or more of amino acids 118, 122-139, 145, 159, 180, 183, 184, 231, and 244. In another embodiment, an amino acid substitution at position 131 of P2X4 reduces or eliminates antibody binding to a human P2X4 polypeptide. In another embodiment, the serine at position 131 of human P2X4 is substituted by Asparagine.

In one embodiment of the previous aspect, the antibody or fragment thereof contains:

a. a heavy chain variable region CDR1 containing a sequence  $X_1X_2X_3X_4X_5$ , where  $X_1$  is G, N, S, D, or R;  $X_2$  is Y, A, H, F, or S;  $X_3$  is A, W, Y, S, G, F, W, E, D, or P;  $X_4$  is M, I, W, L, I, F, or V;  $X_5$  is S, G, T, H, or N; and/or

b. a heavy chain variable region CDR2 containing a sequence

$X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}X_{14}X_{15}X_{16}$ , where  $X_1$  is A, R, I, T, E, S, A, V, W, N, G, E, R, or Y;  $X_2$  is I or M;  $X_3$  is S, K, Y, D, N, W, or I;  $X_4$  is S, D, G, H, N, R, Y, or V;  $X_5$  is G, D, S, F, N, R, F, D, or T;  $X_6$  is G, S, N, or T;  $X_7$  is S, T, D, Y, N, A, E, M, F, or D;  $X_8$  is T, I, K, or A;  $X_9$  is Y, D, R, N, G, Q, E, H, or K;  $X_{10}$  is Y, Q, S, or V;  $X_{11}$  is A, S, N, or V;  $X_{12}$  is D, A, P, R, or Q;  $X_{13}$  is S, P, K, or N;  $X_{14}$  is V, F, L, or A;  $X_{15}$  is K, Q, or E;  $X_{16}$  is G, S, A, or D; and/or

c. a heavy chain variable region CDR3 containing a sequence  $X_1X_2X_3X_4X_5X_6X_7X_8$ ,  $X_1$  is E, N, D, R, K, G, S, A, Y, V, P, or H;  $X_2$  is E, L, R, Q, T, G, F, P, Y, K, A, S, V, or F;  $X_3$  is R, A, T, G, V, S, M, W, Y, D, H, N, E, L, or I;  $X_4$  is G, L, R, D, T, G, Y, S, E, F, Q, C, I, M, V, N, K, or P;  $X_5$  is S, G, Y, D, W, T, S, N, I, D, V, E, or C;  $X_6$  is Y, A, S, W, T, L, G, E, F, K, V, I, or D;  $X_7$  is D, E, or G; and  $X_8$  is Y, S, V, L, M, Q, I, S, I, H, F, or D. In one embodiment, the heavy chain variable region CDR2 optionally contains an insertion of 1-3 amino acids,  $X_aX_bX_c$  between amino acids  $X_3$  and  $X_4$ , where  $X_a$  is G, S, P, W, Y, E, A, R, or N; and  $X_bX_c$  are KT,

respectively. In another embodiment, the heavy chain variable region CDR3 optionally contains an insertion of 1-14 amino acids  $X_a$ - $X_n$ , where  $X_a$  is F, R, S, Y, L, D, G, V, I, T, or A;  $X_b$  is G, R, Y, F, T, D, S, G, V, M, D, or R;  $X_c$  is F, W, A, G, T, I, S, F, Y, C, L, V, R, or N;  $X_d$  is S, F, M, G, Y, L, S, A, D, L, R, V, C, or S;  $X_e$  is G, Y, S, T, P, F, Y, R, A, E, G, Q, N, or L;  $X_f$  is Y, N, G, T, R, F, A, M, W, P, or V;  $X_g$  is Y, M, S, V, F, A, P, S, D, R, H, P, E, or R;  $X_h$  is Y, G, M, F, G, P, V, F, H, T, or G;  $X_i$  is T, I, G, R, or F;  $X_j$  is Y, G, H, or E;  $X_k$  is Y, G, F, or N;  $X_l$  is F, or N;  $X_m$  is Y; and  $X_n$  is F. In one embodiment, the heavy chain variable region CDR1 contains the sequence  $SYX_1MX_2$ , where  $X_1$  is A, W, Y, S, G, F, E, D, or P and  $X_2$  is S, G, T, H, or N. In another embodiment, the heavy chain variable region CDR1 contains the sequence XYAMS, where X is S, D, G, N or R; SXAMS, where X is Y, A, H, F, or S; SYXMS, where X is A, W, Y, S, G, F, E, D, P; SYAXS, where X is M, I, W, L, F, or V; SYAMX, where X is S, G, T, H, or N. In another embodiment, the heavy chain variable region CDR1 contains amino acids SYAMS. In another embodiment, the heavy chain variable region CDR2 contains the sequence AISGSGGSTYYADSVKG; or AISGSGGSTYYADSVEG. In yet another embodiment, the heavy chain variable region CDR3 contains the sequence DWYFDL or NWYLDL. In still another embodiment, the antibody or fragment thereof contains, a. a light chain variable region CDR1 containing a sequence  $X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}$ , where  $X_1$  is T, G, R, S, or Q;  $X_2$  is G, A, or L;  $X_3$  is S, T, D, or H;  $X_4$  is S, N, K, A, Q, T, or V;  $X_5$  is G, I, L, S, or D;  $X_6$  is A, G, R, P, I, D, S, E, T;  $X_7$  is G, N, M, D, K, S, R, Y, or T;  $X_8$  is Y, K, F, Q, S, N, Y, D, H, or R;  $X_9$  is D, N, Y, W, F, M, G, or S;  $X_{10}$  is V, A, L, I, G, or P;  $X_{11}$  is H, T, S, Y, A, Q, Y, N, or F;

b. a light chain variable region CDR2 containing a sequence:  $X_1X_2X_3X_4X_5X_6X_7$ , where  $X_1$  is G, Y, Q, K, N, D, R, A, or E;  $X_2$  is N, D, K, A, V, G, or T;  $X_3$  is N, S, T, I, K, Y, or D;  $X_4$  is N, D, Y, K, E, T, N, S, or Q;  $X_5$  is R, or L;  $X_6$  is P, E, A, S, or Q;  $X_7$  is S, P, or T;

c. a light chain variable region CDR3 containing a sequence  $X_1X_2X_3X_4X_5X_6X_7X_8X_9$ ,  $X_1$  is Q, N, A, G, D, S, or L;  $X_2$  is S, V, A, Q, T, L, or H;  $X_3$  is Y, W, R, A, S, Q, T, or G;  $X_4$  is D, Y, I, N, M, or H;  $X_5$  is T, M, S, N, D, R, G, or K;  $X_6$  is N, T, S, G, F, L or D;  $X_7$  is L, T, G, P, A, I, or N;  $X_8$  is K, W, V, I, P, G, L, R, or Y;  $X_9$  is V, L, or T. In one embodiment, the light chain variable region CDR1 optionally contains an insertion of between 1 and 3 amino acids  $X_a$ - $X_c$  between  $X_4$  and  $X_5$ , where  $X_a$  is S or G;  $X_b$  is N, D or S; and  $X_c$  is I or V. In another embodiment, the light chain variable region CDR3 optionally contains an insertion of between 1 and 3 amino acids  $X_a$ - $X_c$  between  $X_7$  and  $X_8$ , where  $X_a$  is D, N, A, T, S, I or H;  $X_b$  is H, Y, G,

A, R, L, S, or P; X<sub>c</sub> is S. In still another embodiment, the light chain variable region CDR1 contains one of the following sequences: S G D K L; S G S S S N I G; S G D A L; R A S Q G I S S W L A; and R A S Q G I S R W L A. In another embodiment, the light chain variable region CDR2 contains one of the following sequences: G X X Y R P S, where X is T, S, K or K D S E R P S; K A S T L E S; Q D X K R P S, where X is D or T; and Q D I E R P S. In another embodiment, the light chain variable region CDR3 contains one of the following sequences: Q Q S Y S T P W T or S S G T Y V V.

In various embodiments of the above aspects, the antibody contains a heavy chain variable region CDR1, CDR2, and CDR3. In other embodiments of the above aspects, the antibody contains a light chain variable region CDR1, CDR2, and CDR3. In other embodiments of the above aspects the antibody contains a heavy chain variable region CDR1, CDR2, and CDR3, and a light chain variable region CDR1, CDR2, and CDR3. In other embodiments of the above aspects the antibody is a phage display derived antibody selected from any one or more of Antibody Nos. 1-34. In particular embodiments, the antibody is Antibody No. 5, 8, 11, 18, 29, or 33.

In another embodiment of the above aspect, the antibody or fragment thereof contains:

a. a heavy chain variable region CDR1 containing a sequence: X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>X<sub>5</sub>, where X<sub>1</sub> is S, N, D, T, A, or R; X<sub>2</sub> is G, Y, or F; X<sub>3</sub> is Y, H, S, G, D, or F; X<sub>4</sub> is D, V, or I; X<sub>5</sub> is N, H, C, R, S or is absent;

b. a heavy chain variable region CDR2 containing a sequence: X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>X<sub>8</sub>X<sub>9</sub>X<sub>10</sub>X<sub>11</sub>X<sub>12</sub>X<sub>13</sub>X<sub>14</sub>X<sub>15</sub>X<sub>16</sub>, where X<sub>1</sub> is M, V, L, I, A, G, or T; X<sub>2</sub> is G or I; X<sub>3</sub> is Y, W, N, or C; X<sub>4</sub> is Y, G, D, or W; X<sub>5</sub> is S, D, or E; X<sub>6</sub> is G or D; X<sub>7</sub> is S, Y, N, or I; X<sub>8</sub> is T, P, or K; X<sub>9</sub> is N, A, G, D, or V; X<sub>10</sub> is Y or F; X<sub>11</sub> is N; X<sub>12</sub> is P, S, or E; X<sub>13</sub> is S, A, or N; X<sub>14</sub> is L or F; X<sub>15</sub> is K; X<sub>16</sub> is S, G, or N;

c. a heavy chain variable region CDR3 containing a sequence: X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>X<sub>8</sub>, where X<sub>1</sub> is G, S, A, or R; X<sub>2</sub> is M, G, Y, S, L, R, or V; X<sub>3</sub> is M, D, I, V, H, M, or S; X<sub>4</sub> is V, Y, M, W, or S; X<sub>5</sub> is L, Y, S or absent; X<sub>6</sub> is I, D, V, T, G, S or absent; X<sub>7</sub> is P, G, D, S, or A; and X<sub>8</sub> is N, Y, or T. In one embodiment, the heavy chain variable region CDR1 optionally contains amino acids X<sub>6</sub> and X<sub>7</sub>, which are V and S, respectively. In another embodiment, the heavy chain variable region CDR2 optionally contains an insertion of amino acids X<sub>a</sub> and X<sub>b</sub> between X<sub>3</sub> and X<sub>4</sub>, where X<sub>a</sub> is I or P and X<sub>b</sub> is S. In another embodiment, the heavy chain variable

region CDR3 optionally contains an insertion of between 1 and 6 amino acids Xa-Xf between X<sub>6</sub> and X<sub>7</sub>, where Xa is G, T, D, or Y; Xb is S, A, G, or F; Xc is Y, V, P, or F; Xd is Y or F; Xe is Y; and Xf is E, F, or G. In another embodiment, the heavy chain variable region CDR1 contains the sequence S G Y D; S G S D; or S G F D. In another embodiment, the heavy chain variable region CDR2 contains the sequence: M G Y I S Y S; V I W G D G S T A; S T A Y N S; or S T N Y N P. In one embodiment, the heavy chain variable region CDR3 contains the sequence G M M V L I; G V S S L S; or G S Y Y Y X, where X is E, G, or F.

In another embodiment of the above aspect, the antibody or fragment thereof contains:

a. a light chain variable region CDR1 containing a sequence:

10 X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>X<sub>8</sub>X<sub>9</sub>X<sub>10</sub>X<sub>11</sub> where X<sub>1</sub> is K, Q, or R; X<sub>2</sub> is A or T; X<sub>3</sub> is S, R, or N; X<sub>4</sub> is K or Q; X<sub>5</sub> is S, D, R, N, L, or I; X<sub>6</sub> is I or S; X<sub>7</sub> is T, G, V, or N; X<sub>8</sub> is N, S, H, or K; X<sub>9</sub> is Y or W; X<sub>10</sub> is L, M, or I; X<sub>11</sub> is A, S, or Y;

b. a light chain variable region CDR2 containing a sequence: X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>, where X<sub>1</sub> is S, D, E, or Y; X<sub>2</sub> is G, A, or T; X<sub>3</sub> is S or T; X<sub>4</sub> is T, S, K, or A; X<sub>5</sub> is L; X<sub>6</sub> is Q, A, or V;

15 X<sub>7</sub> is S or D;

c. a light chain variable region CDR3 containing a sequence: X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>X<sub>8</sub>X<sub>9</sub> where X<sub>1</sub> is Q, L, or H; X<sub>2</sub> is Q or K; X<sub>3</sub> is Y, A, W, or T; X<sub>4</sub> is Y, H, S, or D; X<sub>5</sub> is E, S, R, T, or N; X<sub>6</sub> is K, N, T, L, or H; X<sub>7</sub> is P; X<sub>8</sub> is Y, W, L, N, P, or R; and X<sub>9</sub> is T. In one embodiment, the light chain variable region CDR1 contains the sequence K A S K X I T, where X is X, L, or I; or Q A S Q D I G N W L. In another embodiment, the light chain variable region CDR2 contains the sequence S G S T L Q S; D A T S L A D; or D A T T L A D. In another embodiment, the light chain variable region CDR3 contains the sequence Q Q Y Y E K P X T or Q Q Y Y E N P X T where X is Y or L.

25 In another series of embodiments the antibody or fragment thereof comprises a VH comprising:

a. a heavy chain variable region CDR1 containing a sequence: S X<sub>1</sub> A M S where X<sub>1</sub> is Y or F;

b. a heavy chain variable region CDR2 containing a sequence: A I S G S G X<sub>1</sub> S T Y Y A D S V K G where X<sub>1</sub> is S or G;

30 c. a heavy chain variable region CDR3 containing a sequence:

X<sub>1</sub>X<sub>2</sub>D X<sub>3</sub>W S X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>X<sub>8</sub>T A F D L, where X<sub>1</sub> is H, D or Q; X<sub>2</sub> is W, M, F, H, or R;

X<sub>3</sub> is W, Y or F; X<sub>4</sub> is T, N, G, or P; X<sub>5</sub> is R, A, S, G, or Y; X<sub>6</sub> is S, P, N or T;  
and X<sub>7</sub> is G, S, R, or K: X<sub>8</sub> is P, M, A or L

optionally in combination with a VL comprising

- a. a light chain variable region CDR1 comprising the sequence SGDALPRQYAY
- b. a light chain variable region CDR2 comprising the sequence KDSXRPS where X is E or F.
- c. a light chain variable region CDR3 comprising the sequence QSADSSGTYXV where X is V or A.

In various embodiments of the above aspects, the antibody contains a heavy chain variable region CDR1, CDR2, and CDR3. In other embodiments of the above aspects, the antibody contains a light chain variable region CDR1, CDR2, and CDR3. In still other  
embodiments of the above aspects, the antibody contains a heavy chain variable region CDR1, CDR2, and CDR3, and a light chain variable region CDR1, CDR2, and CDR3. In particular  
embodiments, the antibody is a hybridoma derived antibody selected from any one or more of  
Antibody Nos. 35-48.

In various embodiments of the above aspects, the antigen binding fragment thereof is a  
single chain antibody, a single chain variable fragment (scFv), a Fab fragment, or a F(ab')<sub>2</sub>  
fragment.

In another aspect, the invention provides a polynucleotide encoding the antibody or  
antigen binding fragment thereof of any of the above aspects.

In another aspect, the invention provides a vector containing the polynucleotide of the  
previous aspect.

In still another aspect, the invention provides a host cell containing the vector of the  
previous aspect.

In another aspect, the invention provides a method for treating neuropathic pain, the  
method involving administering to a patient in need thereof an antibody or antigen binding  
fragment thereof according to any of the above aspects. In one embodiment, the method  
comprises administering to a patient in need thereof an effective amount of an antibody or

antigen binding fragment thereof that specifically binds P2X4 and modulates its ion channel function. In one embodiment, the antibody or antigen binding fragment thereof is administered by intrathecal delivery.

In another aspect, the invention provides a method for the large scale production of a recombinant P2X4 polypeptide, the method involving expressing a human P2X4 protein in an SF9 cell at 27°C for 72 hours; extracting the P2X4 protein by solubilizing in a buffer containing n-Dodecyl-beta-D-Maltoside, n-Dodecyl thio-Maltoside, CHAPS, and the Cholesteryl Hemisuccinate; then isolating the solubilized protein. In one embodiment, the SF9 cells were infected with baculovirus particles with a multiplicity of infection of 2 at a cell density of 2 x 10E6 cells/ml. In another embodiment, the proteins are purified using affinity and size exclusion chromatography. In another embodiment, the purified protein is maintained in a buffer containing 50 mM Tris-HCl pH 8.0, 600 mM NaCl, 10% glycerol, 0.025% n-Dodecyl-beta-D-Maltoside, 0.0125% n-Dodecyl thio-Maltoside, 0.0075% CHAPS, and 0.0015% Cholesteryl Hemisuccinate.

In another embodiment, the method generates milligram quantities of purified P2X4 human polypeptide. In another embodiment, the majority of the P2X4 protein is in the trimeric form.

In another aspect, the invention provides a recombinant human P2X4 polypeptide produced according to the method of any previous aspect. In one embodiment, at least about 65%-75% of the polypeptide is in the trimeric form.

Other features and advantages of the invention will be apparent from the detailed description, and from the claims.

### Definitions

Unless defined otherwise, all technical and scientific terms used herein have the meaning commonly understood by a person skilled in the art to which this invention belongs. The following references provide one of skill with a general definition of many of the terms used in this invention: Singleton et al., Dictionary of Microbiology and Molecular Biology (2nd ed. 1994); The Cambridge Dictionary of Science and Technology (Walker ed., 1988); The Glossary of Genetics, 5th Ed., R. Rieger et al. (eds.), Springer Verlag (1991); and Hale & Marham, The

Harper Collins Dictionary of Biology (1991). As used herein, the following terms have the meanings ascribed to them below, unless specified otherwise.

By “P2X purinoceptor 4 (P2RX4 or P2X4) polypeptide” is meant a purinergic receptor protein or fragment thereof having at least about 85% or greater amino acid identity to the amino

acid sequence provided at NCBI Accession No. Q99571 and having P2X4 biological activity. P2X4 biological activity includes  $\text{Ca}^{2+}/\text{Na}^{+}$  conducting activity in response to ATP binding and/or P2X4 antibody binding. An exemplary human P2X4 sequence is provided below:

```

5      magccaalaa flfeydtpri vlirsrkvgl mnravqlil ayvigwvfww ekgyqetdsv 61
      vssvttkvkg vavtntsklg friwdvadyv ipaqeenslf vmtnviltmn qtqglcpeip 121
      dattvcksda sctagsagth sngvstgrcv afngsvktce vaawcpvedd thvpqpafk 181
      aaenftllvk nniwypkfnf skrnlpnit ttylksciyd aktdpfcipif rlgkivenag 241
      hsfqdmaveg gimgiqvnwd cnldraaslc lprysfrrld trdvehnvsp gynfrfakyy 301
10     rdlagneqrt likaygirfd iivfgkagkf diiptminig sglallgmat vlcdiivlyc 361
      mkkrllyyrek kykyvedyeq glaseldq

```

In embodiments of the invention, a human P2X4 polypeptide has at least about 65%, 70%, 80%, 85%, 90%, 95%, or even 100% identity to NCBI Accession No. Q99571. In other embodiments, the invention provides P2X4 polypeptides comprising one or more amino acid substitutions relative to the Q99571 reference sequence, including for example: E95Q, V105M, G114D, A122V, S131N, A151P, G154R, L303P, and N306K.

An exemplary murine P2X purinoceptor 4 is provided at NCBI Accession No. Q9JJX6, which has the following sequence:

```

      magccsvlgs flfeydtpri vlirsrkvgl mnrvvqlil ayvigwvfww ekgyqetdsv 61
      vssvttkakg vavtntsqlg friwdvadyv vpaqeenslf imtnmivtvn qtqgtcpeip 121
20     dktsicdsda nctlgssdth ssgigtgrcv pfnasvktce vaawcpvend agvptpafk 181
      aaenftllvk nniwypkfnf skrnlpnit tsylksciyn artdpfcipif rlgqivadag 241
      hsfqemaveg gimgiqikwd cnldraashc lprysfrrld trdlehnvsp gynfrfakyy 301
      rdlagneqrt ltkaygirfd iivfgkagkf diiptminvg sglallgvat vlcdvivlyc 361
      mkkryyyrdk kykyvedyeq glsgemng

```

25 An exemplary rat P2X purinoceptor 4 sequence is provided at NCBI Accession No. P51577, which has the following sequence:

```

      magccsvlgs flfeydtpri vlirsrkvgl mnravqlil ayvigwvfww ekgyqetdsv 61
      vssvttkakg vavtntsqlg friwdvadyv ipaqeenslf imtnmivtvn qtqstcpeip 121
30     dktsicnsda dctpgsvdth ssgvatgrcv pfnesvktce vaawcpvend vgvptpafk 181
      aaenftllvk nniwypkfnf skrnlpnit tsylksciyn aqtdpfcipif rlgativedag 241
      hsfqemaveg gimgiqikwd cnldraaslc lprysfrrld trdlehnvsp gynfrfakyy 301
      rdlagkeqrt ltkaygirfd iivfgkagkf diiptminvg sglallgvat vlcdvivlyc 361
      mkkkyyrdrk kykyvedyeq glsgemng

```

35 An exemplary cynomologus monkey (e.g. macaque) P2X purinoceptor 4 sequence, which has the following sequence:

```

      magccaalaa flfeydtpri vlirsrkvgl mnravqlil ayvigwvfww ekgyqetdsv 61
      vssvttkvkg vavtntsklg friwdvadyv ipaqgenslf vmtnmiltmn qtqdlcpeip 121

```

dvttvcksda nctagsagth sngvstgrev pfnrsvktce vaawcpvedd thvpqpaflk 181  
 aaenftllvk nniwypkfnf skrnlpnit ttylksciyd aktdpfcpiif rlgkivenag 241  
 hsfqdmaveg gimgiqvnwd cnldraaslc lprysfrld trdvehnvsp gynfrfakyy 301  
 rdpagkeqrt likaygirfd iivfgkagkf diiptminig sglallgmat vlcdiivlyc 361  
 5 mkkrllyrek kykyvedyeq glaseldp

By "P2X4 nucleic acid molecule" is meant a polynucleotide encoding a P2X4  
 polypeptide or fragment thereof. An exemplary human P2X4 polynucleotide sequence is  
 10 provided at NCBI Accession No. NM\_002560, the sequence of which follows:

1 aagtgctggg atgacaggtg tgagccaccg cccccggccc ctgccccgcc ttttgaagga  
 61 gccttttcgtc ctcaagggcg aggccactcc cccccgcga gttccatgcc ccctagaggg  
 121 tcatcggttc cgacggggag gtggcgccct cccccgggcc cggggccccg accgcccgtg  
 181 ctgcctcett cggggccctc ctccgcgatg acggcgccgc cagcaggcca ggcggactgg  
 15 241 gcgggggtcc gagcggggac tgggaccag accgactagg ggactgggag cgggcggcgc  
 301 ggccatggcg ggtgctgctg ccgcgctggc ggccttcctg ttcgagtacg acacgcgcgc  
 361 catcgctgctc atccgcagcc gcaaagtggg gctcatgaac cgcgccgtgc aactgctcat  
 421 cctggcctac gtcatcgggt ggggtgttgt gtgggaaaag ggctaccagg aaactgactc  
 481 cgtggtcagc tccgttacga ccaaggtcaa gggcgtggct gtgaccaaca cttctaaact  
 20 541 tggattccgg atctgggatg tggcggatta tgtgatacca gctcaggagg aaaactccct  
 601 cttegtcatg accaacgtga tcctcaccat gaaccagaca cagggcctgt gcccgcagat  
 661 tccagatgcg accactgtgt gtaaatcaga tgccagctgt actgccggct ctgccggcac  
 721 ccacagcaac ggagtctcaa caggcaggtg cgtagctttc aacgggtctg tcaagacgtg  
 781 tgagggtggcg gcctggtgcc cgggtggagga tgacacacac gtgccacaac ctgctttttt  
 25 841 aaaggctgca gaaaacttca ctcttttggg taagaacaac atctggtatc ccaaatttaa  
 901 tttcagcaag aggaatatcc ttcccaacat caccactact tacctcaagt cgtgcattta  
 961 tgatgctaaa acagatccct tctgccccat attccgtctt ggcaaaatag tggagaacgc  
 1021 aggacacagt ttccaggaca tggcctgga gggaggcatc atgggcatcc aggtcaactg  
 1081 ggactgcaac ctggacagag ccgcctccct ctgcttgccc aggtactcct tccgcgcct  
 30 1141 cgatacagcg gacgttgagc acaacgtatc tcctggctac aatttcagggt ttgccaagta  
 1201 ctacagagac ctggctggca acgagcagcg cacgctcatc aaggcctatg gcatccgctt  
 1261 cgacatcatt gtgtttggga aggcaggga atttgacatc atccccacta tgatcaacat  
 1321 cggctctggc ctggcactgc taggcctggc gaccgtgctg tgtgacatca tagtcctcta  
 1381 ctgcatgaag aaaagactct actatcggga gaagaaatat aaatatgtgg aagattacga  
 35 1441 gcagggtcct gctagtgagc tggaccagtg aggcctaccc cacacctggg ctctccacag  
 1501 ccccatcaaa gaacagagag gaggaggagg gagaaatggc caccacatca cccagagaa  
 1561 atttctggaa tctgattgag tctccactcc acaagcactc agggttcccc agcagctcct  
 1621 gtgtgttgtg tgcaggatct gtttgccac tcggcccagg aggtcagcag tctgttcttg  
 1681 gctgggtcaa ctctgctttt cccgcaacct ggggttgtcg ggggagcgt ggcccgcgc  
 40 1741 agtggcactg ctgtggcttt cagggtgga gctggctttg ctcagaagcc tcctgtctcc

1801 agctctctcc aggcacaggcc cagtcctctg aggcacggcg gctctgttca agcactttat  
 1861 gcggcagggg aggccgcctg gctgcagtca ctagacttgt agcaggcctg ggctgcaggg  
 1921 ttccccccga ccattccctg cagccatgcg gcagagctgg catttctcct cagagaagcg  
 1981 ctgtgctaag gtgatcgagg accagacatt aaagcgtgat tttcttaaaa aaaaaaaaaa  
 2041 aaa

By "P2X4 biological activity" is meant ion channel conducting activity or ion channel mediated changes in cytosolic calcium levels.

By "ameliorate" is meant decrease, suppress, attenuate, diminish, arrest, or stabilize the development or progression of a disease.

The term "antibody," as used in this disclosure, refers to an immunoglobulin or a fragment or a derivative thereof, and encompasses any polypeptide comprising an antigen-binding site, regardless of whether it is produced *in vitro* or *in vivo*. The term includes, but is not limited to, polyclonal, monoclonal, monospecific, polyspecific, non-specific, humanized, single-chain, chimeric, synthetic, recombinant, hybrid, mutated, and grafted antibodies. Unless otherwise modified by the term "intact," as in "intact antibodies," for the purposes of this disclosure, the term "antibody" also includes antibody fragments such as Fab, F(ab')<sub>2</sub>, Fv, scFv, Fd, dAb, and other antibody fragments that retain antigen-binding function, i.e., the ability to bind a P2X4 polypeptide specifically. Typically, such fragments would comprise an antigen-binding domain.

The terms "antigen-binding domain," "antigen-binding fragment," and "binding fragment" refer to a part of an antibody molecule that comprises amino acids responsible for the specific binding between the antibody and the antigen. In instances, where an antigen is large, the antigen-binding domain may only bind to a part of the antigen. A portion of the antigen molecule that is responsible for specific interactions with the antigen-binding domain is referred to as "epitope" or "antigenic determinant." In particular embodiments, an antigen-binding domain comprises an antibody light chain variable region (V<sub>L</sub>) and an antibody heavy chain variable region (V<sub>H</sub>), however, it does not necessarily have to comprise both. For example, a so-called Fd antibody fragment consists only of a V<sub>H</sub> domain, but still retains some antigen-binding function of the intact antibody.

Binding fragments of an antibody are produced by recombinant DNA techniques, or by enzymatic or chemical cleavage of intact antibodies. Binding fragments include Fab, Fab', F(ab')<sub>2</sub>, Fv, and single-chain antibodies. An antibody other than a "bispecific" or "bifunctional"

antibody is understood to have each of its binding sites identical. Digestion of antibodies with the enzyme, papain, results in two identical antigen-binding fragments, known also as "Fab" fragments, and a "Fc" fragment, having no antigen-binding activity but having the ability to crystallize. Digestion of antibodies with the enzyme, pepsin, results in the a F(ab')<sub>2</sub> fragment in which the two arms of the antibody molecule remain linked and comprise two-antigen binding sites. The F(ab')<sub>2</sub> fragment has the ability to crosslink antigen. "Fv" when used herein refers to the minimum fragment of an antibody that retains both antigen-recognition and antigen-binding sites. "Fab" when used herein refers to a fragment of an antibody that comprises the constant domain of the light chain and the CHI domain of the heavy chain.

The term "mAb" refers to monoclonal antibody. Antibodies of the invention comprise without limitation whole native antibodies, bispecific antibodies; chimeric antibodies; Fab, Fab', single chain V region fragments (scFv), fusion polypeptides, and unconventional antibodies.

In this disclosure, "comprises," "comprising," "containing" and "having" and the like can have the meaning ascribed to them in U.S. Patent law and can mean "includes," "including," and the like; "consisting essentially of" or "consists essentially" likewise has the meaning ascribed in U.S. Patent law and the term is open-ended, allowing for the presence of more than that which is recited so long as basic or novel characteristics of that which is recited is not changed by the presence of more than that which is recited, but excludes prior art embodiments.

"Detect" refers to identifying the presence, absence or amount of the analyte to be detected. In one embodiment, an antibody of the invention or fragment thereof is used to detect the presence or level of a P2X<sub>4</sub> polypeptide.

By "detectable label" is meant a composition that when linked to a molecule of interest renders the latter detectable, via spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include radioactive isotopes, magnetic beads, metallic beads, colloidal particles, fluorescent dyes, electron-dense reagents, enzymes (for example, as commonly used in an ELISA), biotin, digoxigenin, or haptens.

By "disease" is meant any condition or disorder that damages or interferes with the normal function of a cell, tissue, or organ. Examples of diseases include neuropathic pain, particularly pain associated with P2X<sub>4</sub> channel activity or the activity of a pathway responsive to P2X<sub>4</sub>.

The term “effective amount” refers to a dosage or amount of an agent that is sufficient to reduce the activity of a P2X4 polypeptide to result in amelioration of symptoms in a patient or to achieve a desired biological outcome. Desired biological outcomes include, for example, the amelioration of chronic pain or a symptom thereof, modulation of P2X4 biological activity, or the modulation of a pathway responsive to P2X4 activity.

The term “isolated” refers to a molecule that is substantially free of other elements present in its natural environment. For instance, an isolated protein is substantially free of cellular material or other proteins from the cell or tissue source from which it is derived. The term “isolated” also refers to preparations where the isolated protein is sufficiently pure to be administered as a pharmaceutical composition, or at least 70-80% (w/w) pure, more preferably, at least 80-90% (w/w) pure, even more preferably, 90-95% pure; and, most preferably, at least 95%, 96%, 97%, 98%, 99%, or 100% (w/w) pure.

By “fragment” is meant a portion of a polypeptide or nucleic acid molecule. This portion contains, preferably, at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of the entire length of the reference nucleic acid molecule or polypeptide. In a particular embodiment, a fragment of a P2X4 polypeptide may contain 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, or 300 amino acids.

By “reference” is meant a standard of comparison.

A “reference sequence” is a defined sequence used as a basis for sequence comparison. A reference sequence may be a subset of or the entirety of a specified sequence; for example, a segment of a full-length cDNA or gene sequence, or the complete cDNA or gene sequence. For polypeptides, the length of the reference polypeptide sequence will generally be at least about 16 amino acids, preferably at least about 20 amino acids, more preferably at least about 25 amino acids, and even more preferably about 35 amino acids, about 50 amino acids, or about 100 amino acids. For nucleic acids, the length of the reference nucleic acid sequence will generally be at least about 50 nucleotides, preferably at least about 60 nucleotides, more preferably at least about 75 nucleotides, and even more preferably about 100 nucleotides or about 300 nucleotides or any integer thereabout or therebetween.

The term “repertoire” refers to a genetically diverse collection of nucleotides derived wholly or partially from sequences that encode expressed immunoglobulins. The sequences are generated by *in vivo* rearrangement of, e.g., V, D, and J segments for H chains and, e.g., V and J

segment for L chains. Alternatively, the sequences may be generated from a cell line by *in vitro* stimulation, in response to which the rearrangement occurs. Alternatively, part or all of the sequences may be obtained by combining, e.g., unrearranged V segments with D and J segments, by nucleotide synthesis, randomised mutagenesis, and other methods, e.g., as disclosed in U.S.

5 Pat. No. 5,565,332.

By “specifically binds” is meant an agent (*e.g.*, antibody) that recognizes and binds a molecule (*e.g.*, polypeptide), but which does not substantially recognize and bind other molecules in a sample, for example, a biological sample. For example, two molecules that specifically bind form a complex that is relatively stable under physiologic conditions. Specific  
10 binding is characterized by a high affinity and a low to moderate capacity as distinguished from nonspecific binding which usually has a low affinity with a moderate to high capacity. Typically, binding is considered specific when the affinity constant  $K_A$  is higher than  $10^7 \text{ M}^{-1}$ , or more preferably higher than  $10^8 \text{ M}^{-1}$ .

The strength of the binding between P2X4 and an antibody can be measured using, for  
15 example, an enzyme-linked immunoadsorption assay (ELISA), radio-immunoassay (RIA), or surface plasmon resonance-based technology (*e.g.*, Biacore), all of which are techniques well known in the art. If necessary, non-specific binding can be reduced without substantially affecting specific binding by varying the binding conditions. The appropriate binding conditions such as concentration of antibodies, ionic strength of the solution, temperature, time allowed for  
20 binding, concentration of a blocking agent (*e.g.*, serum albumin, milk casein), etc., may be optimized by a skilled artisan using routine techniques.

Unless specifically stated or obvious from context, as used herein, the term “about” is understood as within a range of normal tolerance in the art, for example within 2 standard deviations of the mean. About can be understood as within 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%,  
25 2%, 1%, 0.5%, 0.1%, 0.05%, or 0.01% of the stated value. Unless otherwise clear from context, all numerical values provided herein are modified by the term about.

The recitation of a listing of chemical groups in any definition of a variable herein includes definitions of that variable as any single group or combination of listed groups. The recitation of an embodiment for a variable or aspect herein includes that embodiment as any  
30 single embodiment or in combination with any other embodiments or portions thereof.

Any compositions or methods provided herein can be combined with one or more of any of the other compositions and methods provided herein.

### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1A-1D shows an analysis of Antibody Nos. 1, 11, 29, and 33 binding to human P2X4 variants.

Figure 2 provides the VH & VL sequences of Antibody Nos. 1-34, which were identified using phage display technology.

Figure 3 provides a summary of P2X4 orthologue binding properties of antibodies identified using phage display selection (antibodies 1 to 34) and a summary of their functional effects measured by electrophysiology assays and reported as fraction of control current. Key: + indicates that binding was observed in FMAT assay; - indicates that no binding was observed in FMAT assay; NT indicates that the antibody was not tested in the assay.

Figure 4 shows results of the antibodies 5, 8, 11, 18, 29, and 33 screened in electrophysiology assays. Each of these antibodies was identified as a P2X4 antagonist. Peak agonist induced inward current in response to 3  $\mu$ M ATP in the presence of antibody is indicated as a fraction of control current in the absence of antibody at human or cynomolgus (cyno) P2X4.

Figure 5 provides a summary of P2X4 orthologue binding properties of antibodies isolated from hybridomas (Antibody Nos. 35-48) and a summary of their functional effects measured by electrophysiology assays and reported as fraction of control current.

Figure 6 provides the VH & VL sequences of Antibody Nos. 35-48.

Figure 7 provides a summary of results of binding assays for 252 antibodies (Antibody Nos. 35-286) isolated using hybridoma technology and a summary of their functional effects measured by electrophysiology assays and reported as fraction of control current.

Figure 8A-8F shows whole cell current traces obtained using QPatch 16X showing the agonist response (indicated temporally by the grey bar) before (black trace) and after (grey trace) addition of antibodies. Traces are superimposed for comparison. Dotted line indicates zero current. P2X4 species investigated is indicated where appropriate by (m, mouse) (hu, human).

Figure 8A, 8D, 8E, 8F show activity against huP2X4. Figures 8B and 8C show activity against mP2X4.

Figure 9 shows schematically an extracellular view of predicted P2X4 trimer-Antibody No. 11 Fv complex structure. In particular, Figure 9 illustrates the bipartite epitope-paratope interface – Antibody No. 11 VHCDRs-P2X4 protomer 1 head (major interface - large dotted circle); Antibody No. 11 VLCDRs-P2X4 protomer 2 right flipper (minor interface - small dotted circle). Three Antibody No. 11 molecules can potentially bind the same P2X4 trimer molecule. The two Fab arms of Antibody No. 11 are not likely to engage the same P2X4 trimer molecule. Antibody No. 11 is predicted to bind a P2X heteromer across the epitope formed by two P2X4 subunits.

Figure 10 provides alignments of human, cyno, mouse and rat P2X4 sequences. The head region of the protein is indicated. Amino acids within the predicted epitope are also indicated.

Figure 11 shows the effect of P2X4 antibody Nos. 38 and 208 and an isotype control antibody (NIP228 TM) dosed intra-theically (5 µg per mouse) on reversal of peripheral nerve ligation (PNL)-induced mechanical hyperalgesia as measured by the ipsilateral/contralateral ratio of paw withdrawal threshold in response to paw pressure ( $n = 9-10$  per group). Data analysed using 2 way ANOVA with time and treatment as dependant factors. Subsequent statistical significance obtained using Tukey's Post Hoc test. \*  $P < 0.05$ ; \*\*\*  $P < 0.001$  - Op + NIP228 TM vs Op + Antibody 208: +  $P < 0.05$ ; ++  $P < 0.01$ ; +++  $P < 0.001$  - Op + NIP228 TM vs Op + Antibody 38

Figure 12 provides an alignment of the VH & VL sequences of Antibody Nos. 287 to 315, which are derived from Antibody 11.

Figure 13 provides the VH & VL sequences of Antibody Nos. 208 and 316 to 321

Figure 14 shows the effect of antibody Nos. 11, 300 and 312 on huP2X4 currents recorded on Qpatch 16X. The black trace indicates the ATP response prior to IgG addition whereas the grey trace indicates the ATP response after incubation with IgG. The dashed line indicates the zero current level and the grey bar indicates the time at which ATP was added to the cell bathing solution. Traces are overlayed for comparison. Dose response curves are plotted with normalised current values as described in Example 14 and represent mean  $\pm$  SEM,  $n = 4$ .

Figure 15 summarises  $IC_{50}$  values for optimised versions of Antibody 11 at huP2X4 using either FLIPR or Qpatch 16X. Values are geometric means.

Figure 16 summarises IC<sub>50</sub> values for antibodies 38, 43, 46 & 208 at murineP2X4 and/or huP2X4 expressed in HEK 293F cells obtained on Qpatch 16X.

Figure 17 summarises the effect of antibodies 38, 43, 46 & 208 on mouse microglial P2X4 currents measured on Qpatch 16X.

5 Figure 18 shows exemplary electrophysiology current traces from mouse microglia pretreated with either the control antibody NIP 228 or antibody 208 (0.33 mg/ml). The grey bar indicates the time at which ATP (30  $\mu$ M) was added to the cells and the dotted line indicates the zero current level.

Figure 19 shows example IC<sub>50</sub> curves obtained with two of the anti-P2X4 antibodies in the ATP stimulated calcium response assay.

Figure 20 shows IC<sub>50</sub> curves (mean  $\pm$  SEM) for antibodies 46, 38 and 208 obtained from mouse microglia assayed on FLIPR. Mean IC<sub>50</sub> values are presented below.

Figure 21 shows exemplar electrophysiology current traces from human monocyte derived macrophages. Time at which ATP was added to the cells is indicated by the open box.

15 Dotted line indicates zero current.

Figure 22 summarises the steady state inward current from human monocyte derived macrophages in response to ATP (30  $\mu$ M).

Figure 23 summarises the effect of antibodies 319-321 on huP2X4 currents.

20

### DESCRIPTION OF THE SEQUENCES

| SEQ ID | Antibody | Description |
|--------|----------|-------------|
| 1      | 1        | VH DNA      |
| 2      | 1        | VH PRT      |
| 3      | 1        | CDR1 PRT    |
| 4      | 1        | CDR2 PRT    |
| 5      | 1        | CDR3 PRT    |

|    |   |         |
|----|---|---------|
| 6  | 1 | FW1 PRT |
| 7  | 1 | FW2 PRT |
| 8  | 1 | FW3 PRT |
| 9  | 1 | FW4 PRT |
| 10 | 1 | VL DNA  |
| 11 | 1 | VL PRT  |

|    |   |          |
|----|---|----------|
| 12 | 1 | CDR1 PRT |
| 13 | 1 | CDR2 PRT |
| 14 | 1 | CDR3 PRT |
| 15 | 1 | FW1 PRT  |
| 16 | 1 | FW2 PRT  |
| 17 | 1 | FW3 PRT  |

|    |   |             |
|----|---|-------------|
| 18 | 1 | FW4<br>PRT  |
| 19 | 5 | VH<br>DNA   |
| 20 | 5 | VH<br>PRT   |
| 21 | 5 | CDR1<br>PRT |
| 22 | 5 | CDR2<br>PRT |
| 23 | 5 | CDR3<br>PRT |
| 24 | 5 | FW1<br>PRT  |
| 25 | 5 | FW2<br>PRT  |
| 26 | 5 | FW3<br>PRT  |
| 27 | 5 | FW4<br>PRT  |
| 28 | 5 | VL<br>DNA   |
| 29 | 5 | VL<br>PRT   |
| 30 | 5 | CDR1<br>PRT |
| 31 | 5 | CDR2<br>PRT |
| 32 | 5 | CDR3<br>PRT |
| 33 | 5 | FW1<br>PRT  |
| 34 | 5 | FW2<br>PRT  |
| 35 | 5 | FW3<br>PRT  |
| 36 | 5 | FW4<br>PRT  |
| 37 | 8 | VH<br>DNA   |
| 38 | 8 | VH<br>PRT   |
| 39 | 8 | CDR1<br>PRT |
| 40 | 8 | CDR2<br>PRT |

|    |    |             |
|----|----|-------------|
| 41 | 8  | CDR3<br>PRT |
| 42 | 8  | FW1<br>PRT  |
| 43 | 8  | FW2<br>PRT  |
| 44 | 8  | FW3<br>PRT  |
| 45 | 8  | FW4<br>PRT  |
| 46 | 8  | VL<br>DNA   |
| 47 | 8  | VL<br>PRT   |
| 48 | 8  | CDR1<br>PRT |
| 49 | 8  | CDR2<br>PRT |
| 50 | 8  | CDR3<br>PRT |
| 51 | 8  | FW1<br>PRT  |
| 52 | 8  | FW2<br>PRT  |
| 53 | 8  | FW3<br>PRT  |
| 54 | 8  | FW4<br>PRT  |
| 55 | 11 | VH<br>DNA   |
| 56 | 11 | VH<br>PRT   |
| 57 | 11 | CDR1<br>PRT |
| 58 | 11 | CDR2<br>PRT |
| 59 | 11 | CDR3<br>PRT |
| 60 | 11 | FW1<br>PRT  |
| 61 | 11 | FW2<br>PRT  |
| 62 | 11 | FW3<br>PRT  |
| 63 | 11 | FW4<br>PRT  |

|    |    |             |
|----|----|-------------|
| 64 | 11 | VL<br>DNA   |
| 65 | 11 | VL<br>PRT   |
| 66 | 11 | CDR1<br>PRT |
| 67 | 11 | CDR2<br>PRT |
| 68 | 11 | CDR3<br>PRT |
| 69 | 11 | FW1<br>PRT  |
| 70 | 11 | FW2<br>PRT  |
| 71 | 11 | FW3<br>PRT  |
| 72 | 11 | FW4<br>PRT  |
| 73 | 18 | VH<br>DNA   |
| 74 | 18 | VH<br>PRT   |
| 75 | 18 | CDR1<br>PRT |
| 76 | 18 | CDR2<br>PRT |
| 77 | 18 | CDR3<br>PRT |
| 78 | 18 | FW1<br>PRT  |
| 79 | 18 | FW2<br>PRT  |
| 80 | 18 | FW3<br>PRT  |
| 81 | 18 | FW4<br>PRT  |
| 82 | 18 | VL<br>DNA   |
| 83 | 18 | VL<br>PRT   |
| 84 | 18 | CDR1<br>PRT |
| 85 | 18 | CDR2<br>PRT |
| 86 | 18 | CDR3<br>PRT |

|     |    |             |
|-----|----|-------------|
| 87  | 18 | FW1<br>PRT  |
| 88  | 18 | FW2<br>PRT  |
| 89  | 18 | FW3<br>PRT  |
| 90  | 18 | FW4<br>PRT  |
| 91  | 29 | VH<br>DNA   |
| 92  | 29 | VH<br>PRT   |
| 93  | 29 | CDR1<br>PRT |
| 94  | 29 | CDR2<br>PRT |
| 95  | 29 | CDR3<br>PRT |
| 96  | 29 | FW1<br>PRT  |
| 97  | 29 | FW2<br>PRT  |
| 98  | 29 | FW3<br>PRT  |
| 99  | 29 | FW4<br>PRT  |
| 100 | 29 | VL<br>DNA   |
| 101 | 29 | VL<br>PRT   |
| 102 | 29 | CDR1<br>PRT |
| 103 | 29 | CDR2<br>PRT |
| 104 | 29 | CDR3<br>PRT |
| 105 | 29 | FW1<br>PRT  |
| 106 | 29 | FW2<br>PRT  |
| 107 | 29 | FW3<br>PRT  |
| 108 | 29 | FW4<br>PRT  |
| 109 | 33 | VH<br>DNA   |

|     |    |             |
|-----|----|-------------|
| 110 | 33 | VH<br>PRT   |
| 111 | 33 | CDR1<br>PRT |
| 112 | 33 | CDR2<br>PRT |
| 113 | 33 | CDR3<br>PRT |
| 114 | 33 | FW1<br>PRT  |
| 115 | 33 | FW2<br>PRT  |
| 116 | 33 | FW3<br>PRT  |
| 117 | 33 | FW4<br>PRT  |
| 118 | 33 | VL<br>DNA   |
| 119 | 33 | VL<br>PRT   |
| 120 | 33 | CDR1<br>PRT |
| 121 | 33 | CDR2<br>PRT |
| 122 | 33 | CDR3<br>PRT |
| 123 | 33 | FW1<br>PRT  |
| 124 | 33 | FW2<br>PRT  |
| 125 | 33 | FW3<br>PRT  |
| 126 | 33 | FW4<br>PRT  |
| 127 | 35 | VH<br>DNA   |
| 128 | 35 | VH<br>PRT   |
| 129 | 35 | CDR1<br>PRT |
| 130 | 35 | CDR2<br>PRT |
| 131 | 35 | CDR3<br>PRT |
| 132 | 35 | FW1<br>PRT  |

|     |    |             |
|-----|----|-------------|
| 133 | 35 | FW2<br>PRT  |
| 134 | 35 | FW3<br>PRT  |
| 135 | 35 | FW4<br>PRT  |
| 136 | 35 | VL<br>DNA   |
| 137 | 35 | VL<br>PRT   |
| 138 | 35 | CDR1<br>PRT |
| 139 | 35 | CDR2<br>PRT |
| 140 | 35 | CDR3<br>PRT |
| 141 | 35 | FW1<br>PRT  |
| 142 | 35 | FW2<br>PRT  |
| 143 | 35 | FW3<br>PRT  |
| 144 | 35 | FW4<br>PRT  |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
| 163 | 37 | VH<br>DNA   |

|     |    |             |
|-----|----|-------------|
| 164 | 37 | VH<br>PRT   |
| 165 | 37 | CDR1<br>PRT |
| 166 | 37 | CDR2<br>PRT |
| 167 | 37 | CDR3<br>PRT |
| 168 | 37 | FW1<br>PRT  |
| 169 | 37 | FW2<br>PRT  |
| 170 | 37 | FW3<br>PRT  |
| 171 | 37 | FW4<br>PRT  |
| 172 | 37 | VL<br>DNA   |
| 173 | 37 | VL<br>PRT   |
| 174 | 37 | CDR1<br>PRT |
| 175 | 37 | CDR2<br>PRT |
| 176 | 37 | CDR3<br>PRT |
| 177 | 37 | FW1<br>PRT  |
| 178 | 37 | FW2<br>PRT  |
| 179 | 37 | FW3<br>PRT  |
| 180 | 37 | FW4<br>PRT  |
| 181 | 38 | VH<br>DNA   |
| 182 | 38 | VH<br>PRT   |
| 183 | 38 | CDR1<br>PRT |
| 184 | 38 | CDR2<br>PRT |
| 185 | 38 | CDR3<br>PRT |
| 186 | 38 | FW1<br>PRT  |

|     |    |             |
|-----|----|-------------|
| 187 | 38 | FW2<br>PRT  |
| 188 | 38 | FW3<br>PRT  |
| 189 | 38 | FW4<br>PRT  |
| 190 | 38 | VL<br>DNA   |
| 191 | 38 | VL<br>PRT   |
| 192 | 38 | CDR1<br>PRT |
| 193 | 38 | CDR2<br>PRT |
| 194 | 38 | CDR3<br>PRT |
| 195 | 38 | FW1<br>PRT  |
| 196 | 38 | FW2<br>PRT  |
| 197 | 38 | FW3<br>PRT  |
| 198 | 38 | FW4<br>PRT  |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
| 217 | 40 | VH<br>DNA   |

[illegible]

|     |    |             |
|-----|----|-------------|
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
|     |    |             |
| 253 | 42 | VH<br>DNA   |
| 254 | 42 | VH<br>PRT   |
| 255 | 42 | CDR1<br>PRT |
| 256 | 42 | CDR2<br>PRT |
| 257 | 42 | CDR3<br>PRT |
| 258 | 42 | FW1<br>PRT  |
| 259 | 42 | FW2<br>PRT  |
| 260 | 42 | FW3<br>PRT  |
| 261 | 42 | FW4<br>PRT  |
| 262 | 42 | VL<br>DNA   |
| 263 | 42 | VL<br>PRT   |
| 264 | 42 | CDR1<br>PRT |
| 265 | 42 | CDR2<br>PRT |
| 266 | 42 | CDR3<br>PRT |
| 267 | 42 | FW1<br>PRT  |
| 268 | 42 | FW2<br>PRT  |
| 269 | 42 | FW3<br>PRT  |
| 270 | 42 | FW4<br>PRT  |
| 271 | 43 | VH          |

|     |    |             |
|-----|----|-------------|
|     |    | DNA         |
| 272 | 43 | VH<br>PRT   |
| 273 | 43 | CDR1<br>PRT |
| 274 | 43 | CDR2<br>PRT |
| 275 | 43 | CDR3<br>PRT |
| 276 | 43 | FW1<br>PRT  |
| 277 | 43 | FW2<br>PRT  |
| 278 | 43 | FW3<br>PRT  |
| 279 | 43 | FW4<br>PRT  |
| 280 | 43 | VL<br>DNA   |
| 281 | 43 | VL<br>PRT   |
| 282 | 43 | CDR1<br>PRT |
| 283 | 43 | CDR2<br>PRT |
| 284 | 43 | CDR3<br>PRT |
| 285 | 43 | FW1<br>PRT  |
| 286 | 43 | FW2<br>PRT  |
| 287 | 43 | FW3<br>PRT  |
| 288 | 43 | FW4<br>PRT  |
| 289 | 44 | VH<br>DNA   |
| 290 | 44 | VH<br>PRT   |
| 291 | 44 | CDR1<br>PRT |
| 292 | 44 | CDR2<br>PRT |
| 293 | 44 | CDR3<br>PRT |

|     |    |             |
|-----|----|-------------|
| 294 | 44 | FW1<br>PRT  |
| 295 | 44 | FW2<br>PRT  |
| 296 | 44 | FW3<br>PRT  |
| 297 | 44 | FW4<br>PRT  |
| 298 | 44 | VL<br>DNA   |
| 299 | 44 | VL<br>PRT   |
| 300 | 44 | CDR1<br>PRT |
| 301 | 44 | CDR2<br>PRT |
| 302 | 44 | CDR3<br>PRT |
| 303 | 44 | FW1<br>PRT  |
| 304 | 44 | FW2<br>PRT  |
| 305 | 44 | FW3<br>PRT  |
| 306 | 44 | FW4<br>PRT  |
| 307 | 45 | VH<br>DNA   |
| 308 | 45 | VH<br>PRT   |
| 309 | 45 | CDR1<br>PRT |
| 310 | 45 | CDR2<br>PRT |
| 311 | 45 | CDR3<br>PRT |
| 312 | 45 | FW1<br>PRT  |
| 313 | 45 | FW2<br>PRT  |
| 314 | 45 | FW3<br>PRT  |
| 315 | 45 | FW4<br>PRT  |
| 316 | 45 | VL<br>DNA   |

|     |    |             |
|-----|----|-------------|
| 317 | 45 | VL<br>PRT   |
| 318 | 45 | CDR1<br>PRT |
| 319 | 45 | CDR2<br>PRT |
| 320 | 45 | CDR3<br>PRT |
| 321 | 45 | FW1<br>PRT  |
| 322 | 45 | FW2<br>PRT  |
| 323 | 45 | FW3<br>PRT  |
| 324 | 45 | FW4<br>PRT  |
| 325 | 46 | VH<br>DNA   |
| 326 | 46 | VH<br>PRT   |
| 327 | 46 | CDR1<br>PRT |
| 328 | 46 | CDR2<br>PRT |
| 329 | 46 | CDR3<br>PRT |
| 330 | 46 | FW1<br>PRT  |
| 331 | 46 | FW2<br>PRT  |
| 332 | 46 | FW3<br>PRT  |
| 333 | 46 | FW4<br>PRT  |
| 334 | 46 | VL<br>DNA   |
| 335 | 46 | VL<br>PRT   |
| 336 | 46 | CDR1<br>PRT |
| 337 | 46 | CDR2<br>PRT |
| 338 | 46 | CDR3<br>PRT |
| 339 | 46 | FW1<br>PRT  |

|     |    |             |
|-----|----|-------------|
| 340 | 46 | FW2<br>PRT  |
| 341 | 46 | FW3<br>PRT  |
| 342 | 46 | FW4<br>PRT  |
| 343 | 47 | VH<br>DNA   |
| 344 | 47 | VH<br>PRT   |
| 345 | 47 | CDR1<br>PRT |
| 346 | 47 | CDR2<br>PRT |
| 347 | 47 | CDR3<br>PRT |
| 348 | 47 | FW1<br>PRT  |
| 349 | 47 | FW2<br>PRT  |
| 350 | 47 | FW3<br>PRT  |
| 351 | 47 | FW4<br>PRT  |
| 352 | 47 | VL<br>DNA   |
| 353 | 47 | VL<br>PRT   |
| 354 | 47 | CDR1<br>PRT |
| 355 | 47 | CDR2<br>PRT |
| 356 | 47 | CDR3<br>PRT |
| 357 | 47 | FW1<br>PRT  |
| 358 | 47 | FW2<br>PRT  |
| 359 | 47 | FW3<br>PRT  |
| 360 | 47 | FW4<br>PRT  |
| 361 | 48 | VH<br>DNA   |
| 362 | 48 | VH<br>PRT   |

|     |     |             |
|-----|-----|-------------|
| 363 | 48  | CDR1<br>PRT |
| 364 | 48  | CDR2<br>PRT |
| 365 | 48  | CDR3<br>PRT |
| 366 | 48  | FW1<br>PRT  |
| 367 | 48  | FW2<br>PRT  |
| 368 | 48  | FW3<br>PRT  |
| 369 | 48  | FW4<br>PRT  |
| 370 | 48  | VL<br>DNA   |
| 371 | 48  | VL<br>PRT   |
| 372 | 48  | CDR1<br>PRT |
| 373 | 48  | CDR2<br>PRT |
| 374 | 48  | CDR3<br>PRT |
| 375 | 48  | FW1<br>PRT  |
| 376 | 48  | FW2<br>PRT  |
| 377 | 48  | FW3<br>PRT  |
| 378 | 48  | FW4<br>PRT  |
| 379 | 287 | VH<br>DNA   |
| 380 | 287 | VH<br>PRT   |
| 381 | 287 | CDR1<br>PRT |
| 382 | 287 | CDR2<br>PRT |
| 383 | 287 | CDR3<br>PRT |
| 384 | 287 | FW1<br>PRT  |
| 385 | 287 | FW2<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 386 | 287 | FW3<br>PRT  |
| 387 | 287 | FW4<br>PRT  |
| 388 | 287 | VL<br>DNA   |
| 389 | 287 | VL<br>PRT   |
| 390 | 287 | CDR1<br>PRT |
| 391 | 287 | CDR2<br>PRT |
| 392 | 287 | CDR3<br>PRT |
| 393 | 287 | FW1<br>PRT  |
| 394 | 287 | FW2<br>PRT  |
| 395 | 287 | FW3<br>PRT  |
| 396 | 287 | FW4<br>PRT  |
| 397 | 288 | VH<br>DNA   |
| 398 | 288 | VH<br>PRT   |
| 399 | 288 | CDR1<br>PRT |
| 400 | 288 | CDR2<br>PRT |
| 401 | 288 | CDR3<br>PRT |
| 402 | 288 | FW1<br>PRT  |
| 403 | 288 | FW2<br>PRT  |
| 404 | 288 | FW3<br>PRT  |
| 405 | 288 | FW4<br>PRT  |
| 406 | 288 | VL<br>DNA   |
| 407 | 288 | VL<br>PRT   |
| 408 | 288 | CDR1<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 409 | 288 | CDR2<br>PRT |
| 410 | 288 | CDR3<br>PRT |
| 411 | 288 | FW1<br>PRT  |
| 412 | 288 | FW2<br>PRT  |
| 413 | 288 | FW3<br>PRT  |
| 414 | 288 | FW4<br>PRT  |
| 415 | 289 | VH<br>DNA   |
| 416 | 289 | VH<br>PRT   |
| 417 | 289 | CDR1<br>PRT |
| 418 | 289 | CDR2<br>PRT |
| 419 | 289 | CDR3<br>PRT |
| 420 | 289 | FW1<br>PRT  |
| 421 | 289 | FW2<br>PRT  |
| 422 | 289 | FW3<br>PRT  |
| 423 | 289 | FW4<br>PRT  |
| 424 | 289 | VL<br>DNA   |
| 425 | 289 | VL<br>PRT   |
| 426 | 289 | CDR1<br>PRT |
| 427 | 289 | CDR2<br>PRT |
| 428 | 289 | CDR3<br>PRT |
| 429 | 289 | FW1<br>PRT  |
| 430 | 289 | FW2<br>PRT  |
| 431 | 289 | FW3<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 432 | 289 | FW4<br>PRT  |
| 433 | 290 | VH<br>DNA   |
| 434 | 290 | VH<br>PRT   |
| 435 | 290 | CDR1<br>PRT |
| 436 | 290 | CDR2<br>PRT |
| 437 | 290 | CDR3<br>PRT |
| 438 | 290 | FW1<br>PRT  |
| 439 | 290 | FW2<br>PRT  |
| 440 | 290 | FW3<br>PRT  |
| 441 | 290 | FW4<br>PRT  |
| 442 | 290 | VL<br>DNA   |
| 443 | 290 | VL<br>PRT   |
| 444 | 290 | CDR1<br>PRT |
| 445 | 290 | CDR2<br>PRT |
| 446 | 290 | CDR3<br>PRT |
| 447 | 290 | FW1<br>PRT  |
| 448 | 290 | FW2<br>PRT  |
| 449 | 290 | FW3<br>PRT  |
| 450 | 290 | FW4<br>PRT  |
| 451 | 291 | VH<br>DNA   |
| 452 | 291 | VH<br>PRT   |
| 453 | 291 | CDR1<br>PRT |
| 454 | 291 | CDR2<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 455 | 291 | CDR3<br>PRT |
| 456 | 291 | FW1<br>PRT  |
| 457 | 291 | FW2<br>PRT  |
| 458 | 291 | FW3<br>PRT  |
| 459 | 291 | FW4<br>PRT  |
| 460 | 291 | VL<br>DNA   |
| 461 | 291 | VL<br>PRT   |
| 462 | 291 | CDR1<br>PRT |
| 463 | 291 | CDR2<br>PRT |
| 464 | 291 | CDR3<br>PRT |
| 465 | 291 | FW1<br>PRT  |
| 466 | 291 | FW2<br>PRT  |
| 467 | 291 | FW3<br>PRT  |
| 468 | 291 | FW4<br>PRT  |
| 469 | 292 | VH<br>DNA   |
| 470 | 292 | VH<br>PRT   |
| 471 | 292 | CDR1<br>PRT |
| 472 | 292 | CDR2<br>PRT |
| 473 | 292 | CDR3<br>PRT |
| 474 | 292 | FW1<br>PRT  |
| 475 | 292 | FW2<br>PRT  |
| 476 | 292 | FW3<br>PRT  |
| 477 | 292 | FW4<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 478 | 292 | VL<br>DNA   |
| 479 | 292 | VL<br>PRT   |
| 480 | 292 | CDR1<br>PRT |
| 481 | 292 | CDR2<br>PRT |
| 482 | 292 | CDR3<br>PRT |
| 483 | 292 | FW1<br>PRT  |
| 484 | 292 | FW2<br>PRT  |
| 485 | 292 | FW3<br>PRT  |
| 486 | 292 | FW4<br>PRT  |
| 487 | 293 | VH<br>DNA   |
| 488 | 293 | VH<br>PRT   |
| 489 | 293 | CDR1<br>PRT |
| 490 | 293 | CDR2<br>PRT |
| 491 | 293 | CDR3<br>PRT |
| 492 | 293 | FW1<br>PRT  |
| 493 | 293 | FW2<br>PRT  |
| 494 | 293 | FW3<br>PRT  |
| 495 | 293 | FW4<br>PRT  |
| 496 | 293 | VL<br>DNA   |
| 497 | 293 | VL<br>PRT   |
| 498 | 293 | CDR1<br>PRT |
| 499 | 293 | CDR2<br>PRT |
| 500 | 293 | CDR3<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 501 | 293 | FW1<br>PRT  |
| 502 | 293 | FW2<br>PRT  |
| 503 | 293 | FW3<br>PRT  |
| 504 | 293 | FW4<br>PRT  |
| 505 | 294 | VH<br>DNA   |
| 506 | 294 | VH<br>PRT   |
| 507 | 294 | CDR1<br>PRT |
| 508 | 294 | CDR2<br>PRT |
| 509 | 294 | CDR3<br>PRT |
| 510 | 294 | FW1<br>PRT  |
| 511 | 294 | FW2<br>PRT  |
| 512 | 294 | FW3<br>PRT  |
| 513 | 294 | FW4<br>PRT  |
| 514 | 294 | VL<br>DNA   |
| 515 | 294 | VL<br>PRT   |
| 516 | 294 | CDR1<br>PRT |
| 517 | 294 | CDR2<br>PRT |
| 518 | 294 | CDR3<br>PRT |
| 519 | 294 | FW1<br>PRT  |
| 520 | 294 | FW2<br>PRT  |
| 521 | 294 | FW3<br>PRT  |
| 522 | 294 | FW4<br>PRT  |
| 523 | 295 | VH<br>DNA   |

|     |     |             |
|-----|-----|-------------|
| 524 | 295 | VH<br>PRT   |
| 525 | 295 | CDR1<br>PRT |
| 526 | 295 | CDR2<br>PRT |
| 527 | 295 | CDR3<br>PRT |
| 528 | 295 | FW1<br>PRT  |
| 529 | 295 | FW2<br>PRT  |
| 530 | 295 | FW3<br>PRT  |
| 531 | 295 | FW4<br>PRT  |
| 532 | 295 | VL<br>DNA   |
| 533 | 295 | VL<br>PRT   |
| 534 | 295 | CDR1<br>PRT |
| 535 | 295 | CDR2<br>PRT |
| 536 | 295 | CDR3<br>PRT |
| 537 | 295 | FW1<br>PRT  |
| 538 | 295 | FW2<br>PRT  |
| 539 | 295 | FW3<br>PRT  |
| 540 | 295 | FW4<br>PRT  |
| 541 | 296 | VH<br>DNA   |
| 542 | 296 | VH<br>PRT   |
| 543 | 296 | CDR1<br>PRT |
| 544 | 296 | CDR2<br>PRT |
| 545 | 296 | CDR3<br>PRT |
| 546 | 296 | FW1<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 547 | 296 | FW2<br>PRT  |
| 548 | 296 | FW3<br>PRT  |
| 549 | 296 | FW4<br>PRT  |
| 550 | 296 | VL<br>DNA   |
| 551 | 296 | VL<br>PRT   |
| 552 | 296 | CDR1<br>PRT |
| 553 | 296 | CDR2<br>PRT |
| 554 | 296 | CDR3<br>PRT |
| 555 | 296 | FW1<br>PRT  |
| 556 | 296 | FW2<br>PRT  |
| 557 | 296 | FW3<br>PRT  |
| 558 | 296 | FW4<br>PRT  |
| 559 | 297 | VH<br>DNA   |
| 560 | 297 | VH<br>PRT   |
| 561 | 297 | CDR1<br>PRT |
| 562 | 297 | CDR2<br>PRT |
| 563 | 297 | CDR3<br>PRT |
| 564 | 297 | FW1<br>PRT  |
| 565 | 297 | FW2<br>PRT  |
| 566 | 297 | FW3<br>PRT  |
| 567 | 297 | FW4<br>PRT  |
| 568 | 297 | VL<br>DNA   |
| 569 | 297 | VL<br>PRT   |

|     |     |             |
|-----|-----|-------------|
| 570 | 297 | CDR1<br>PRT |
| 571 | 297 | CDR2<br>PRT |
| 572 | 297 | CDR3<br>PRT |
| 573 | 297 | FW1<br>PRT  |
| 574 | 297 | FW2<br>PRT  |
| 575 | 297 | FW3<br>PRT  |
| 576 | 297 | FW4<br>PRT  |
| 577 | 298 | VH<br>DNA   |
| 578 | 298 | VH<br>PRT   |
| 579 | 298 | CDR1<br>PRT |
| 580 | 298 | CDR2<br>PRT |
| 581 | 298 | CDR3<br>PRT |
| 582 | 298 | FW1<br>PRT  |
| 583 | 298 | FW2<br>PRT  |
| 584 | 298 | FW3<br>PRT  |
| 585 | 298 | FW4<br>PRT  |
| 586 | 298 | VL<br>DNA   |
| 587 | 298 | VL<br>PRT   |
| 588 | 298 | CDR1<br>PRT |
| 589 | 298 | CDR2<br>PRT |
| 590 | 298 | CDR3<br>PRT |
| 591 | 298 | FW1<br>PRT  |
| 592 | 298 | FW2<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 593 | 298 | FW3<br>PRT  |
| 594 | 298 | FW4<br>PRT  |
| 595 | 299 | VH<br>DNA   |
| 596 | 299 | VH<br>PRT   |
| 597 | 299 | CDR1<br>PRT |
| 598 | 299 | CDR2<br>PRT |
| 599 | 299 | CDR3<br>PRT |
| 600 | 299 | FW1<br>PRT  |
| 601 | 299 | FW2<br>PRT  |
| 602 | 299 | FW3<br>PRT  |
| 603 | 299 | FW4<br>PRT  |
| 604 | 299 | VL<br>DNA   |
| 605 | 299 | VL<br>PRT   |
| 606 | 299 | CDR1<br>PRT |
| 607 | 299 | CDR2<br>PRT |
| 608 | 299 | CDR3<br>PRT |
| 609 | 299 | FW1<br>PRT  |
| 610 | 299 | FW2<br>PRT  |
| 611 | 299 | FW3<br>PRT  |
| 612 | 299 | FW4<br>PRT  |
| 613 | 300 | VH<br>DNA   |
| 614 | 300 | VH<br>PRT   |
| 615 | 300 | CDR1<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 616 | 300 | CDR2<br>PRT |
| 617 | 300 | CDR3<br>PRT |
| 618 | 300 | FW1<br>PRT  |
| 619 | 300 | FW2<br>PRT  |
| 620 | 300 | FW3<br>PRT  |
| 621 | 300 | FW4<br>PRT  |
| 622 | 300 | VL<br>DNA   |
| 623 | 300 | VL<br>PRT   |
| 624 | 300 | CDR1<br>PRT |
| 625 | 300 | CDR2<br>PRT |
| 626 | 300 | CDR3<br>PRT |
| 627 | 300 | FW1<br>PRT  |
| 628 | 300 | FW2<br>PRT  |
| 629 | 300 | FW3<br>PRT  |
| 630 | 300 | FW4<br>PRT  |
| 631 | 302 | VH<br>DNA   |
| 632 | 302 | VH<br>PRT   |
| 633 | 302 | CDR1<br>PRT |
| 634 | 302 | CDR2<br>PRT |
| 635 | 302 | CDR3<br>PRT |
| 636 | 302 | FW1<br>PRT  |
| 637 | 302 | FW2<br>PRT  |
| 638 | 302 | FW3<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 639 | 302 | FW4<br>PRT  |
| 640 | 302 | VL<br>DNA   |
| 641 | 302 | VL<br>PRT   |
| 642 | 302 | CDR1<br>PRT |
| 643 | 302 | CDR2<br>PRT |
| 644 | 302 | CDR3<br>PRT |
| 645 | 302 | FW1<br>PRT  |
| 646 | 302 | FW2<br>PRT  |
| 647 | 302 | FW3<br>PRT  |
| 648 | 302 | FW4<br>PRT  |
| 649 | 303 | VH<br>DNA   |
| 650 | 303 | VH<br>PRT   |
| 651 | 303 | CDR1<br>PRT |
| 652 | 303 | CDR2<br>PRT |
| 653 | 303 | CDR3<br>PRT |
| 654 | 303 | FW1<br>PRT  |
| 655 | 303 | FW2<br>PRT  |
| 656 | 303 | FW3<br>PRT  |
| 657 | 303 | FW4<br>PRT  |
| 658 | 303 | VL<br>DNA   |
| 659 | 303 | VL<br>PRT   |
| 660 | 303 | CDR1<br>PRT |
| 661 | 303 | CDR2<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 662 | 303 | CDR3<br>PRT |
| 663 | 303 | FW1<br>PRT  |
| 664 | 303 | FW2<br>PRT  |
| 665 | 303 | FW3<br>PRT  |
| 666 | 303 | FW4<br>PRT  |
| 667 | 304 | VH<br>DNA   |
| 668 | 304 | VH<br>PRT   |
| 669 | 304 | CDR1<br>PRT |
| 670 | 304 | CDR2<br>PRT |
| 671 | 304 | CDR3<br>PRT |
| 672 | 304 | FW1<br>PRT  |
| 673 | 304 | FW2<br>PRT  |
| 674 | 304 | FW3<br>PRT  |
| 675 | 304 | FW4<br>PRT  |
| 676 | 304 | VL<br>DNA   |
| 677 | 304 | VL<br>PRT   |
| 678 | 304 | CDR1<br>PRT |
| 679 | 304 | CDR2<br>PRT |
| 680 | 304 | CDR3<br>PRT |
| 681 | 304 | FW1<br>PRT  |
| 682 | 304 | FW2<br>PRT  |
| 683 | 304 | FW3<br>PRT  |
| 684 | 304 | FW4<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 685 | 305 | VH<br>DNA   |
| 686 | 305 | VH<br>PRT   |
| 687 | 305 | CDR1<br>PRT |
| 688 | 305 | CDR2<br>PRT |
| 689 | 305 | CDR3<br>PRT |
| 690 | 305 | FW1<br>PRT  |
| 691 | 305 | FW2<br>PRT  |
| 692 | 305 | FW3<br>PRT  |
| 693 | 305 | FW4<br>PRT  |
| 694 | 305 | VL<br>DNA   |
| 695 | 305 | VL<br>PRT   |
| 696 | 305 | CDR1<br>PRT |
| 697 | 305 | CDR2<br>PRT |
| 698 | 305 | CDR3<br>PRT |
| 699 | 305 | FW1<br>PRT  |
| 700 | 305 | FW2<br>PRT  |
| 701 | 305 | FW3<br>PRT  |
| 702 | 305 | FW4<br>PRT  |
| 703 | 306 | VH<br>DNA   |
| 704 | 306 | VH<br>PRT   |
| 705 | 306 | CDR1<br>PRT |
| 706 | 306 | CDR2<br>PRT |
| 707 | 306 | CDR3<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 708 | 306 | FW1<br>PRT  |
| 709 | 306 | FW2<br>PRT  |
| 710 | 306 | FW3<br>PRT  |
| 711 | 306 | FW4<br>PRT  |
| 712 | 306 | VL<br>DNA   |
| 713 | 306 | VL<br>PRT   |
| 714 | 306 | CDR1<br>PRT |
| 715 | 306 | CDR2<br>PRT |
| 716 | 306 | CDR3<br>PRT |
| 717 | 306 | FW1<br>PRT  |
| 718 | 306 | FW2<br>PRT  |
| 719 | 306 | FW3<br>PRT  |
| 720 | 306 | FW4<br>PRT  |
| 721 | 307 | VH<br>DNA   |
| 722 | 307 | VH<br>PRT   |
| 723 | 307 | CDR1<br>PRT |
| 724 | 307 | CDR2<br>PRT |
| 725 | 307 | CDR3<br>PRT |
| 726 | 307 | FW1<br>PRT  |
| 727 | 307 | FW2<br>PRT  |
| 728 | 307 | FW3<br>PRT  |
| 729 | 307 | FW4<br>PRT  |
| 730 | 307 | VL<br>DNA   |

|     |     |             |
|-----|-----|-------------|
| 731 | 307 | VL<br>PRT   |
| 732 | 307 | CDR1<br>PRT |
| 733 | 307 | CDR2<br>PRT |
| 734 | 307 | CDR3<br>PRT |
| 735 | 307 | FW1<br>PRT  |
| 736 | 307 | FW2<br>PRT  |
| 737 | 307 | FW3<br>PRT  |
| 738 | 307 | FW4<br>PRT  |
| 739 | 308 | VH<br>DNA   |
| 740 | 308 | VH<br>PRT   |
| 741 | 308 | CDR1<br>PRT |
| 742 | 308 | CDR2<br>PRT |
| 743 | 308 | CDR3<br>PRT |
| 744 | 308 | FW1<br>PRT  |
| 745 | 308 | FW2<br>PRT  |
| 746 | 308 | FW3<br>PRT  |
| 747 | 308 | FW4<br>PRT  |
| 748 | 308 | VL<br>DNA   |
| 749 | 308 | VL<br>PRT   |
| 750 | 308 | CDR1<br>PRT |
| 751 | 308 | CDR2<br>PRT |
| 752 | 308 | CDR3<br>PRT |
| 753 | 308 | FW1<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 754 | 308 | FW2<br>PRT  |
| 755 | 308 | FW3<br>PRT  |
| 756 | 308 | FW4<br>PRT  |
| 757 | 309 | VH<br>DNA   |
| 758 | 309 | VH<br>PRT   |
| 759 | 309 | CDR1<br>PRT |
| 760 | 309 | CDR2<br>PRT |
| 761 | 309 | CDR3<br>PRT |
| 762 | 309 | FW1<br>PRT  |
| 763 | 309 | FW2<br>PRT  |
| 764 | 309 | FW3<br>PRT  |
| 765 | 309 | FW4<br>PRT  |
| 766 | 309 | VL<br>DNA   |
| 767 | 309 | VL<br>PRT   |
| 768 | 309 | CDR1<br>PRT |
| 769 | 309 | CDR2<br>PRT |
| 770 | 309 | CDR3<br>PRT |
| 771 | 309 | FW1<br>PRT  |
| 772 | 309 | FW2<br>PRT  |
| 773 | 309 | FW3<br>PRT  |
| 774 | 309 | FW4<br>PRT  |
| 775 | 310 | VH<br>DNA   |
| 776 | 310 | VH<br>PRT   |

|     |     |             |
|-----|-----|-------------|
| 777 | 310 | CDR1<br>PRT |
| 778 | 310 | CDR2<br>PRT |
| 779 | 310 | CDR3<br>PRT |
| 780 | 310 | FW1<br>PRT  |
| 781 | 310 | FW2<br>PRT  |
| 782 | 310 | FW3<br>PRT  |
| 783 | 310 | FW4<br>PRT  |
| 784 | 310 | VL<br>DNA   |
| 785 | 310 | VL<br>PRT   |
| 786 | 310 | CDR1<br>PRT |
| 787 | 310 | CDR2<br>PRT |
| 788 | 310 | CDR3<br>PRT |
| 789 | 310 | FW1<br>PRT  |
| 790 | 310 | FW2<br>PRT  |
| 791 | 310 | FW3<br>PRT  |
| 792 | 310 | FW4<br>PRT  |
| 793 | 311 | VH<br>DNA   |
| 794 | 311 | VH<br>PRT   |
| 795 | 311 | CDR1<br>PRT |
| 796 | 311 | CDR2<br>PRT |
| 797 | 311 | CDR3<br>PRT |
| 798 | 311 | FW1<br>PRT  |
| 799 | 311 | FW2<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 800 | 311 | FW3<br>PRT  |
| 801 | 311 | FW4<br>PRT  |
| 802 | 311 | VL<br>DNA   |
| 803 | 311 | VL<br>PRT   |
| 804 | 311 | CDR1<br>PRT |
| 805 | 311 | CDR2<br>PRT |
| 806 | 311 | CDR3<br>PRT |
| 807 | 311 | FW1<br>PRT  |
| 808 | 311 | FW2<br>PRT  |
| 809 | 311 | FW3<br>PRT  |
| 810 | 311 | FW4<br>PRT  |
| 811 | 312 | VH<br>DNA   |
| 812 | 312 | VH<br>PRT   |
| 813 | 312 | CDR1<br>PRT |
| 814 | 312 | CDR2<br>PRT |
| 815 | 312 | CDR3<br>PRT |
| 816 | 312 | FW1<br>PRT  |
| 817 | 312 | FW2<br>PRT  |
| 818 | 312 | FW3<br>PRT  |
| 819 | 312 | FW4<br>PRT  |
| 820 | 312 | VL<br>DNA   |
| 821 | 312 | VL<br>PRT   |
| 822 | 312 | CDR1<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 823 | 312 | CDR2<br>PRT |
| 824 | 312 | CDR3<br>PRT |
| 825 | 312 | FW1<br>PRT  |
| 826 | 312 | FW2<br>PRT  |
| 827 | 312 | FW3<br>PRT  |
| 828 | 312 | FW4<br>PRT  |
| 829 | 313 | VH<br>DNA   |
| 830 | 313 | VH<br>PRT   |
| 831 | 313 | CDR1<br>PRT |
| 832 | 313 | CDR2<br>PRT |
| 833 | 313 | CDR3<br>PRT |
| 834 | 313 | FW1<br>PRT  |
| 835 | 313 | FW2<br>PRT  |
| 836 | 313 | FW3<br>PRT  |
| 837 | 313 | FW4<br>PRT  |
| 838 | 313 | VL<br>DNA   |
| 839 | 313 | VL<br>PRT   |
| 840 | 313 | CDR1<br>PRT |
| 841 | 313 | CDR2<br>PRT |
| 842 | 313 | CDR3<br>PRT |
| 843 | 313 | FW1<br>PRT  |
| 844 | 313 | FW2<br>PRT  |
| 845 | 313 | FW3<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 846 | 313 | FW4<br>PRT  |
| 847 | 314 | VH<br>DNA   |
| 848 | 314 | VH<br>PRT   |
| 849 | 314 | CDR1<br>PRT |
| 850 | 314 | CDR2<br>PRT |
| 851 | 314 | CDR3<br>PRT |
| 852 | 314 | FW1<br>PRT  |
| 853 | 314 | FW2<br>PRT  |
| 854 | 314 | FW3<br>PRT  |
| 855 | 314 | FW4<br>PRT  |
| 856 | 314 | VL<br>DNA   |
| 857 | 314 | VL<br>PRT   |
| 858 | 314 | CDR1<br>PRT |
| 859 | 314 | CDR2<br>PRT |
| 860 | 314 | CDR3<br>PRT |
| 861 | 314 | FW1<br>PRT  |
| 862 | 314 | FW2<br>PRT  |
| 863 | 314 | FW3<br>PRT  |
| 864 | 314 | FW4<br>PRT  |
| 865 | 315 | VH<br>DNA   |
| 866 | 315 | VH<br>PRT   |
| 867 | 315 | CDR1<br>PRT |
| 868 | 315 | CDR2<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 869 | 315 | CDR3<br>PRT |
| 870 | 315 | FW1<br>PRT  |
| 871 | 315 | FW2<br>PRT  |
| 872 | 315 | FW3<br>PRT  |
| 873 | 315 | FW4<br>PRT  |
| 874 | 315 | VL<br>DNA   |
| 875 | 315 | VL<br>PRT   |
| 876 | 315 | CDR1<br>PRT |
| 877 | 315 | CDR2<br>PRT |
| 878 | 315 | CDR3<br>PRT |
| 879 | 315 | FW1<br>PRT  |
| 880 | 315 | FW2<br>PRT  |
| 881 | 315 | FW3<br>PRT  |
| 882 | 315 | FW4<br>PRT  |
| 883 | 316 | VH<br>DNA   |
| 884 | 316 | VH<br>PRT   |
| 885 | 316 | CDR1<br>PRT |
| 886 | 316 | CDR2<br>PRT |
| 887 | 316 | CDR3<br>PRT |
| 888 | 316 | FW1<br>PRT  |
| 889 | 316 | FW2<br>PRT  |
| 890 | 316 | FW3<br>PRT  |
| 891 | 316 | FW4<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 892 | 316 | VL<br>DNA   |
| 893 | 316 | VL<br>PRT   |
| 894 | 316 | CDR1<br>PRT |
| 895 | 316 | CDR2<br>PRT |
| 896 | 316 | CDR3<br>PRT |
| 897 | 316 | FW1<br>PRT  |
| 898 | 316 | FW2<br>PRT  |
| 899 | 316 | FW3<br>PRT  |
| 900 | 316 | FW4<br>PRT  |
| 901 | 317 | VH<br>DNA   |
| 902 | 317 | VH<br>PRT   |
| 903 | 317 | CDR1<br>PRT |
| 904 | 317 | CDR2<br>PRT |
| 905 | 317 | CDR3<br>PRT |
| 906 | 317 | FW1<br>PRT  |
| 907 | 317 | FW2<br>PRT  |
| 908 | 317 | FW3<br>PRT  |
| 909 | 317 | FW4<br>PRT  |
| 910 | 317 | VL<br>DNA   |
| 911 | 317 | VL<br>PRT   |
| 912 | 317 | CDR1<br>PRT |
| 913 | 317 | CDR2<br>PRT |
| 914 | 317 | CDR3<br>PRT |

|     |     |             |
|-----|-----|-------------|
| 915 | 317 | FW1<br>PRT  |
| 916 | 317 | FW2<br>PRT  |
| 917 | 317 | FW3<br>PRT  |
| 918 | 317 | FW4<br>PRT  |
| 919 | 318 | VH<br>DNA   |
| 920 | 318 | VH<br>PRT   |
| 921 | 318 | CDR1<br>PRT |
| 922 | 318 | CDR2<br>PRT |
| 923 | 318 | CDR3<br>PRT |
| 924 | 318 | FW1<br>PRT  |
| 925 | 318 | FW2<br>PRT  |
| 926 | 318 | FW3<br>PRT  |
| 927 | 318 | FW4<br>PRT  |
| 928 | 318 | VL<br>DNA   |
| 929 | 318 | VL<br>PRT   |
| 930 | 318 | CDR1<br>PRT |
| 931 | 318 | CDR2<br>PRT |
| 932 | 318 | CDR3<br>PRT |
| 933 | 318 | FW1<br>PRT  |
| 934 | 318 | FW2<br>PRT  |
| 935 | 318 | FW3<br>PRT  |
| 936 | 318 | FW4<br>PRT  |
| 937 | 319 | VH<br>DNA   |

|     |     |             |
|-----|-----|-------------|
| 938 | 319 | VH<br>PRT   |
| 939 | 319 | CDR1<br>PRT |
| 940 | 319 | CDR2<br>PRT |
| 941 | 319 | CDR3<br>PRT |
| 942 | 319 | FW1<br>PRT  |
| 943 | 319 | FW2<br>PRT  |
| 944 | 319 | FW3<br>PRT  |
| 945 | 319 | FW4<br>PRT  |
| 946 | 319 | VL<br>DNA   |
| 947 | 319 | VL<br>PRT   |
| 948 | 319 | CDR1<br>PRT |
| 949 | 319 | CDR2<br>PRT |
| 950 | 319 | CDR3<br>PRT |
| 951 | 319 | FW1<br>PRT  |
| 952 | 319 | FW2<br>PRT  |
| 953 | 319 | FW3<br>PRT  |
| 954 | 319 | FW4<br>PRT  |
| 955 | 320 | VH<br>DNA   |
| 956 | 320 | VH<br>PRT   |
| 957 | 320 | CDR1<br>PRT |
| 958 | 320 | CDR2<br>PRT |
| 959 | 320 | CDR3<br>PRT |
| 960 | 320 | FW1<br>PRT  |

|     |     |             |
|-----|-----|-------------|
| 961 | 320 | FW2<br>PRT  |
| 962 | 320 | FW3<br>PRT  |
| 963 | 320 | FW4<br>PRT  |
| 964 | 320 | VL<br>DNA   |
| 965 | 320 | VL<br>PRT   |
| 966 | 320 | CDR1<br>PRT |
| 967 | 320 | CDR2<br>PRT |
| 968 | 320 | CDR3<br>PRT |
| 969 | 320 | FW1<br>PRT  |
| 970 | 320 | FW2<br>PRT  |
| 971 | 320 | FW3<br>PRT  |
| 972 | 320 | FW4<br>PRT  |
| 973 | 321 | VH<br>DNA   |
| 974 | 321 | VH<br>PRT   |
| 975 | 321 | CDR1<br>PRT |
| 976 | 321 | CDR2<br>PRT |
| 977 | 321 | CDR3<br>PRT |
| 978 | 321 | FW1<br>PRT  |
| 979 | 321 | FW2<br>PRT  |
| 980 | 321 | FW3<br>PRT  |
| 981 | 321 | FW4<br>PRT  |
| 982 | 321 | VL<br>DNA   |
| 983 | 321 | VL<br>PRT   |

|      |     |             |
|------|-----|-------------|
| 984  | 321 | CDR1<br>PRT |
| 985  | 321 | CDR2<br>PRT |
| 986  | 321 | CDR3<br>PRT |
| 987  | 321 | FW1<br>PRT  |
| 988  | 321 | FW2<br>PRT  |
| 989  | 321 | FW3<br>PRT  |
| 990  | 321 | FW4<br>PRT  |
| 991  | 208 | VH<br>DNA   |
| 992  | 208 | VH<br>PRT   |
| 993  | 208 | CDR1<br>PRT |
| 994  | 208 | CDR2<br>PRT |
| 995  | 208 | CDR3<br>PRT |
| 996  | 208 | FW1<br>PRT  |
| 997  | 208 | FW2<br>PRT  |
| 998  | 208 | FW3<br>PRT  |
| 999  | 208 | FW4<br>PRT  |
| 100  | 208 | VL<br>DNA   |
| 1001 | 208 | VL<br>PRT   |
| 1002 | 208 | CDR1<br>PRT |
| 1003 | 208 | CDR2<br>PRT |
| 1004 | 208 | CDR3<br>PRT |
| 1005 | 208 | FW1<br>PRT  |
| 1006 | 208 | FW2<br>PRT  |

|      |     |            |
|------|-----|------------|
| 1007 | 208 | FW3<br>PRT |
|------|-----|------------|

|      |     |            |
|------|-----|------------|
| 1008 | 208 | FW4<br>PRT |
|------|-----|------------|

## DETAILED DESCRIPTION OF THE INVENTION

As described below, the present invention provides antibodies that specifically bind a P2X4 polypeptide and modulate P2X4 channel activity, recombinant P2X4 polypeptides and methods for generating such polypeptides, as well as compositions and methods for generating anti-P2X4 antibodies, and methods of using P2X4 antibodies for the treatment of neuropathic pain and other indications.

### Recombinant Expression of P2X4

The present invention provides purified isolated recombinant P2X4 polypeptides that form stable trimeric complexes. The invention further provides methods for the large scale production of purified and isolated human and murine P2X4 polypeptides, which is sufficient to produce milligram quantities of P2X4 protein, where the isolated and purified recombinant proteins are predominantly present as stable trimers. The total quantities of P2X4 that were produced for the selection and screening experiments described herein included 6.2 mg hP2X4 and 3.2 mg mP2X4. The production level of purified protein was 0.2 mg/L insect cell culture. As assayed by fluorescent size exclusion chromatography the protein preparation contains 50-75% trimer.

Expression and purification of human-P2X4 with a C-terminal deca Histidine tag in HEK293 cells has been described (Young et al., J. Biol. Chem. 283 (2008) 26241-26251). The purification involved solubilization using dodecylmaltoside detergent and Ni-immobilized metal affinity chromatography. A polyacrylamide gel electrophoretic purification step was required to isolate the trimeric form. Although a fully trimeric preparation of hP2X4 was claimed to have been isolated, the described yield was only 40 µg per 2.5x10<sup>8</sup> cells.

Another example of small scale expression and purification of trimer rat P2X channels (subtypes 2, 4 and 7) has been performed (Antonio et al., Br. J. Pharmacol. 163 (2011) 1069-1077). Rat P2X4 receptors having a C-terminal Hemagglutinin tag were expressed transiently in tsA 201 cells (a sub-clone of HEK293 cells stably expressing the SV40 large T-antigen).

Receptors were solubilized in CHAPS detergent and affinity purified. Compared to expression of P2X2 and P2X7, expression of P2X4 was relatively low. The purified receptors were used in

AFM imaging, which showed trimeric arrangement of the receptors and also double trimers (dimers of trimers).

In another report Sf9 insect cell system was evaluated for expression of human P2X4 and *Dictyostelium discoideum* P2XA (Valente et al., Biochim. Biophys. Acta 1808 (2011) 2859-2866). While the *D. discoideum* P2XA could be obtained in a stable, purified and detergent soluble form, the human P2X4 was reported not to be amenable to be produced in a trimeric form.

The methods present in the prior art uniformly failed to isolate substantial quantities of recombinant P2X4 polypeptides. Moreover, the prior art failed to isolate human P2X4 complexes in milligram quantities where the majority of the isolated proteins were present in trimeric form. In contrast, the methods of the invention, which are suitable for scale up, have allowed milligram scale production of purified recombinant P2X4 polypeptide. The yield of purified P2X4 obtained was 0.2 mg/L insect cell culture medium, corresponding to approximately 8 µg per  $1 \times 10^8$  cells.

For the large scale production of purified P2X4, the human P2X4 and mouse P2X4 receptors were expressed in Sf9 insect cells using a baculovirus expression system. Expression and protein production are not limited to Sf9 insect cell lines, other insect cell and cell lines that support protein production include *Spodoptera frugiperda* Sf21 cells or *Trichoplusia ni* derived cell lines Tn-368 and High-Five™ BTI-TN-5B1-4. To increase protein production, P2X4 expression levels were monitored at the time of harvest, and the quality and homogeneity of the receptors was assessed using a modified size-exclusion chromatography while detecting fluorescence (FSEC) method as described by Backmark et al., (Protein Sci. 22 (2013) 1124-1132). This method is similar to the basic FSEC concept as described by Kawate and Gouaux (Structure 14 (2006) 673-681),, but applied a fluorescent probe that specifically interacts with a Histidine tag on the protein. To achieve the surprising yields reported herein, cells were inoculated at a density of  $1.0 \times 10^6$ /mL in SF900II medium. Cells were infected with a multiplicity of infection of 2 at a cell density of  $2 \times 10^6$  cells/ml. Protein expression was performed at 27°C and cells were harvested 72 hours post infection. These conditions permitted an optimal quantity of the trimeric form of P2X4 to be produced. The homogeneity of protein was unexpected. While the total amount of expressed P2X4 protein increased with longer post

infection times, the quality of the expressed protein as assayed by FSEC did not increase beyond 72 hours.

### Anti-P2X4 Antibodies

5           The disclosure provides anti-P2X4 antibodies that comprise novel antigen-binding fragments. In a particular embodiment, the anti-P2X4 antibody is an anti-P2X4 antibody described herein (e.g., Antibodies 1-48) or a fragment thereof.

          In general, antibodies can be made, for example, using traditional hybridoma techniques (Kohler and Milstein (1975) *Nature*, 256: 495-499), recombinant DNA methods (U.S. Pat. No. 10 4,816,567), or phage display performed with antibody libraries (Clackson, T. and Lowman, H.B. *Phage Display – A Practical Approach*, 2004. Oxford University Press; (2) Thompson, J. et al. *J Mol Biol.* 256(1):77-88, 1996; (3) Osbourn, J.K. et al. *Immunotechnology*, 2(3):181-96, 1996). Exemplary antibodies 35-48 were obtained using hybridoma techniques as described herein. Exemplary antibodies 1-34 were obtained using phage display as described herein. For other 15 antibody production techniques, see also *Antibodies: A Laboratory Manual*, eds. Harlow et al., Cold Spring Harbor Laboratory, 1988. The invention is not limited to any particular source, species of origin, or method of production.

          Intact antibodies, also known as immunoglobulins, are typically tetrameric glycosylated proteins composed of two light (L) chains of approximately 25 kDa each and two heavy (H) 20 chains of approximately 50 kDa each. Two types of light chain, designated as the  $\lambda$  chain and the  $\kappa$  chain, are found in antibodies. Depending on the amino acid sequence of the constant domain of heavy chains, immunoglobulins can be assigned to five major classes: A, D, E, G, and M, and several of these may be further divided into subclasses (isotypes), e.g., IgG<sub>1</sub>, IgG<sub>2</sub>, IgG<sub>3</sub>, IgG<sub>4</sub>, IgA<sub>1</sub>, and IgA<sub>2</sub>.

25           The subunit structures and three-dimensional configurations of different classes of immunoglobulins are well known in the art. For a review of antibody structure, see Harlow et al., *supra*. Briefly, each light chain is composed of an N-terminal variable domain (V<sub>L</sub>) and a constant domain (C<sub>L</sub>). Each heavy chain is composed of an N-terminal variable domain (V<sub>H</sub>), three or four constant domains (C<sub>H</sub>), and a hinge region. The C<sub>H</sub> domain most proximal to V<sub>H</sub> is 30 designated as C<sub>H</sub>1. The V<sub>H</sub> and V<sub>L</sub> domains consist of four regions of relatively conserved sequence called framework regions (FR1, FR2, FR3, and FR4), which form a scaffold for three

regions of hypervariable sequence called complementarity determining regions (CDRs). The CDRs contain most of the residues responsible for specific interactions with the antigen. The three CDRs are referred to as CDR1, CDR2, and CDR3. CDR constituents on the heavy chain are referred to as H1, H2, and H3, while CDR constituents on the light chain are referred to as L1, L2, and L3, accordingly. CDR3 and, particularly H3, are the greatest source of molecular diversity within the antigen-binding domain. H3, for example, can be as short as two amino acid residues or greater than 26. In particular embodiments, a heavy chain CDR3 (H3) comprises between about 4 amino acids (see, for example, Ab No. 2) and 22 amino acids (see, for example, Ab Nos. 20 and 34).

The Fab fragment (Fragment antigen-binding) consists of the  $V_H$ - $C_H1$  and  $V_L$ - $C_L$  domains covalently linked by a disulfide bond between the constant regions. To overcome the tendency of non-covalently linked  $V_H$  and  $V_L$  domains in the Fv to dissociate when co-expressed in a host cell, a so-called single chain (sc) Fv fragment (scFv) can be constructed. In a scFv, a flexible and adequately long polypeptide links either the C-terminus of the  $V_H$  to the N-terminus of the  $V_L$  or the C-terminus of the  $V_L$  to the N-terminus of the  $V_H$ . Most commonly, a 15-residue (Gly<sub>4</sub>Ser)<sub>3</sub> peptide is used as a linker, but other linkers are also known in the art.

Antibody diversity is a result of combinatorial assembly of multiple germline genes encoding variable regions and a variety of somatic events. The somatic events include recombination of variable gene segments with diversity (D) and joining (J) gene segments to make a complete  $V_H$  region and the recombination of variable and joining gene segments to make a complete  $V_L$  region. The recombination process itself is imprecise, resulting in the loss or addition of amino acids at the V(D)J junctions. These mechanisms of diversity occur in the developing B cell prior to antigen exposure. After antigenic stimulation, the expressed antibody genes in B cells undergo somatic mutation.

Based on the estimated number of germline gene segments, the random recombination of these segments, and random  $V_H$ - $V_L$  pairing, up to  $1.6 \times 10^7$  different antibodies could be produced (Fundamental Immunology, 3rd ed., ed. Paul, Raven Press, New York, N.Y., 1993). When other processes that contribute to antibody diversity (such as somatic mutation) are taken into account, it is thought that upwards of  $1 \times 10^{10}$  different antibodies could be potentially generated (Immunoglobulin Genes, 2<sup>nd</sup> ed., eds. Jonio et al., Academic Press, San Diego, Calif., 1995). Because of the many processes involved in antibody diversity, it is highly unlikely that

independently generated antibodies will have identical or even substantially similar amino acid sequences in the CDRs.

The disclosure provides novel CDRs derived from human immunoglobulin gene libraries. The structure for carrying a CDR will generally be an antibody heavy or light chain or a portion thereof, in which the CDR is located at a location corresponding to the CDR of naturally occurring  $V_H$  and  $V_L$ . The structures and locations of immunoglobulin variable domains may be determined, for example, as described in Kabat et al., Sequences of Proteins of Immunological Interest, No. 91-3242, National Institutes of Health Publications, Bethesda, Md., 1991.

The amino acid sequences of anti-P2X4 antibodies 1-48, 208, and 287 to 321, including their  $V_H$  and  $V_L$  domains are set forth in the Figures and described herein.

Anti-P2X4 antibodies may optionally comprise antibody constant regions or parts thereof. For example, a  $V_L$  domain may have attached, at its C terminus, antibody light chain constant domains including human  $C_k$  or  $C_\lambda$  chains. Similarly, a specific antigen-binding domain based on a  $V_H$  domain may have attached all or part of an immunoglobulin heavy chain derived from any antibody isotope, e.g., IgG, IgA, IgE, and IgM and any of the isotope subclasses, which include but are not limited to, IgG<sub>1</sub> and IgG<sub>4</sub>. The DNA and amino acid sequences for the C-terminal fragment of are well known in the art (see, e.g., Kabat et al., Sequences of Proteins of Immunological Interest, No. 91-3242, National Institutes of Health Publications, Bethesda, Md., 1991).

Certain embodiments comprise a  $V_H$  and/or  $V_L$  domain of an Fv fragment from a P2X4 antibody. Further embodiments comprise at least one CDR of any of these  $V_H$  and  $V_L$  domains. Antibodies, comprising at least one of the CDR sequences set forth for Antibody Nos. 1-48 are encompassed within the scope of this invention. In one particular embodiment, an antibody of the invention comprises CDR3 of  $V_H$ .

In certain embodiments, the  $V_H$  and/or  $V_L$  domains may be germlined, i.e., the framework regions (FRs) of these domains are mutated using conventional molecular biology techniques to match those produced by the germline cells. In other embodiments, the framework sequences remain diverged from the consensus germline sequences.

In certain embodiments, the antibodies specifically bind an epitope within the extracellular domain of human P2X4. In certain embodiments, the antibodies specifically bind

an epitope within the extracellular domain of human or mouse P2X4, with an affinity of more than  $10^6 \text{ M}^{-1}$ , more than  $10^7 \text{ M}^{-1}$ , or more than  $10^8 \text{ M}^{-1}$ .

It is contemplated that antibodies of the invention may also bind with other proteins, including, for example, recombinant proteins comprising all or a portion of the P2X4  
5 extracellular domain.

One of ordinary skill in the art will recognize that the antibodies of this invention may be used to detect, measure, and inhibit proteins that differ somewhat from P2X4. The antibodies are expected to retain the specificity of binding so long as the target protein comprises a sequence which is at least about 60%, 70%, 80%, 90%, 95%, or more identical to any sequence of at least  
10 100, 80, 60, 40, or 20 of contiguous amino acids of P2X4 (NCBI Ref. No. Q99571). The percent identity is determined by standard alignment algorithms such as, for example, Basic Local Alignment Tool (BLAST) described in Altshul et al. (1990) J. Mol. Biol., 215: 403-410, the algorithm of Needleman et al. (1970) J. Mol. Biol., 48: 444-453, or the algorithm of Meyers et al. (1988) Comput. Appl. Biosci., 4: 11-17.

In addition to the sequence homology analyses, epitope mapping (see, e.g., Epitope Mapping Protocols, ed. Morris, Humana Press, 1996) and secondary and tertiary structure analyses can be carried out to identify specific 3D structures assumed by the disclosed antibodies and their complexes with antigens. An example of such a 3D structure is provided for Antibody No. 11. Such methods include, but are not limited to, X-ray crystallography (Engstrom (1974)  
20 Biochem. Exp. Biol., 11:7-13) and computer modeling of virtual representations of the presently disclosed antibodies (Fletterick et al. (1986) Computer Graphics and Molecular Modeling, in Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.).

## 25 **Derivatives**

This disclosure provides methods for obtaining antibodies specific for P2X4. CDRs in such antibodies are not limited to the specific sequences of  $V_H$  and  $V_L$  identified herein, and may include variants of these sequences that retain the ability to specifically bind P2X4. Such variants may be derived from the sequences listed herein by a skilled artisan using techniques  
30 well known in the art. For example, amino acid substitutions, deletions, or additions, can be made in the FRs and/or in the CDRs. While changes in the FRs are usually designed to improve

stability and immunogenicity of the antibody, changes in the CDRs are typically designed to increase affinity of the antibody for its target. Variants of FRs also include naturally occurring immunoglobulin allotypes. Such affinity-increasing changes may be determined empirically by routine techniques that involve altering the CDR and testing the affinity of the antibody for its target. For example, conservative amino acid substitutions can be made within any one of the disclosed CDRs. Various alterations can be made according to the methods described in Antibody Engineering, 2<sup>nd</sup> ed., Oxford University Press, ed. Borrebaeck, 1995. These include, but are not limited to, nucleotide sequences that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a “silent” change. For example, the nonpolar amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine, and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs (see Table 1). Furthermore, any native residue in the polypeptide may also be substituted with alanine (see, e.g., MacLennan et al. (1998) Acta Physiol. Scand. Suppl. 643:55-67; Sasaki et al. (1998) Adv. Biophys. 35:1-24).

**Table 1.**

| Original Residues | Exemplary Substitutions                 | Typical Substitutions |
|-------------------|-----------------------------------------|-----------------------|
| Ala (A)           | Val, Leu, Ile                           | Val                   |
| Arg (R)           | Lys, Gln, Asn                           | Lys                   |
| Asn (N)           | Gln                                     | Gln                   |
| Asp (D)           | Glu                                     | Glu                   |
| Cys (C)           | Ser, Ala                                | Ser                   |
| Gln (Q)           | Asn                                     | Asn                   |
| Gly (G)           | Pro, Ala                                | Ala                   |
| His (H)           | Asn, Gln, Lys, Arg                      | Arg                   |
| Ile (I)           | Leu, Val, Met, Ala, Phe, Norleucine     | Leu                   |
| Leu (L)           | Norleucine, Ile, Val, Met, Ala, Phe     | Ile                   |
| Lys (K)           | Arg, 1,4-Diamino-butyric Acid, Gln, Asn | Arg                   |
| Met (M)           | Leu, Phe, Ile                           | Leu                   |
| Phe (F)           | Leu, Val, Ile, Ala, Tyr                 | Leu                   |
| Pro (P)           | Ala                                     | Gly                   |
| Ser (S)           | Thr, Ala, Cys                           | Thr                   |
| Thr (T)           | Ser                                     | Ser                   |
| Trp (W)           | Tyr, Phe                                | Tyr                   |
| Tyr (Y)           | Trp, Phe, Thr, Ser                      | Phe                   |
| Val (V)           | Ile, Met, Leu, Phe, Ala, Norleucine     | Leu                   |

Derivatives and analogs of antibodies of the invention can be produced by various techniques well known in the art, including recombinant and synthetic methods (Maniatis (1990) Molecular Cloning, A Laboratory Manual, 2<sup>nd</sup> ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., and Bodansky et al. (1995) The Practice of Peptide Synthesis, 2<sup>nd</sup> ed., Springer Verlag, Berlin, Germany).

In one embodiment, a method for making a V<sub>H</sub> domain which is an amino acid sequence variant of a V<sub>H</sub> domain of the invention comprises a step of adding, deleting, substituting, or inserting one or more amino acids in the amino acid sequence of the presently disclosed V<sub>H</sub> domain, optionally combining the V<sub>H</sub> domain thus provided with one or more V<sub>L</sub> domains, and testing the V<sub>H</sub> domain or V<sub>H</sub>/V<sub>L</sub> combination or combinations for a specific binding to P2X4 or and, optionally, testing the ability of such antigen-binding domain to modulate P2X4 activity, for example, using an electrophysiology assay described herein. The V<sub>L</sub> domain may have an amino acid sequence that is identical or is substantially identical to a polypeptide of the invention.

An analogous method can be employed in which one or more sequence variants of a V<sub>L</sub> domain disclosed herein are combined with one or more V<sub>H</sub> domains.

A further aspect of the disclosure provides a method of preparing an antigen-binding fragment that specifically binds with P2X4. The method comprises:

- 5 (a) providing a starting repertoire of nucleic acids encoding a V<sub>H</sub> domain that either includes a CDR3 to be replaced or lacks a CDR3 encoding region;
- (b) combining the repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set out herein for a V<sub>H</sub> CDR3 (i.e., H3) such that the donor nucleic acid is inserted into the CDR3 region in the repertoire, so as to provide a  
10 product repertoire of nucleic acids encoding a V<sub>H</sub> domain;
- (c) expressing the nucleic acids of the product repertoire;
- (d) selecting a binding fragment specific for P2X4; and
- (e) recovering the specific binding fragment or nucleic acid encoding it.

Again, an analogous method may be employed in which a V<sub>L</sub> CDR3 (i.e., L3) of the  
15 invention is combined with a repertoire of nucleic acids encoding a V<sub>L</sub> domain, which either include a CDR3 to be replaced or lack a CDR3 encoding region. The donor nucleic acid may be selected from nucleic acids encoding an amino acid sequence substantially as set out in Antibody Nos. 1-48.

A sequence encoding a CDR of the invention (e.g., CDR3) may be introduced into a  
20 repertoire of variable domains lacking the respective CDR (e.g., CDR3), using recombinant DNA technology, for example, using methodology described by Marks et al. (Bio/Technology (1992) 10: 779-783). In particular, consensus primers directed at or adjacent to the 5' end of the variable domain area can be used in conjunction with consensus primers to the third framework region of human V<sub>H</sub> genes to provide a repertoire of V<sub>H</sub> variable domains lacking a CDR3. The  
25 repertoire may be combined with a CDR3 of a particular antibody. Using analogous techniques, the CDR3-derived sequences may be shuffled with repertoires of V<sub>H</sub> or V<sub>L</sub> domains lacking a CDR3, and the shuffled complete V<sub>H</sub> or V<sub>L</sub> domains combined with a cognate V<sub>L</sub> or V<sub>H</sub> domain to make the P2X4-specific antibodies of the invention. The repertoire may then be displayed in a suitable host system such as the phage display system described herein or as described in  
30 WO92/01047 so that suitable antigen-binding fragments can be selected.

Analogous shuffling or combinatorial techniques are also disclosed by Stemmer (Nature (1994) 370: 389-391), who describes the technique in relation to a  $\beta$ -lactamase gene but observes that the approach may be used for the generation of antibodies.

In further embodiments, one may generate novel  $V_H$  or  $V_L$  regions carrying one or more sequences derived from the sequences disclosed herein using random mutagenesis of one or more selected  $V_H$  and/or  $V_L$  genes. One such technique, error-prone PCR, is described by Gram et al. (Proc. Nat. Acad. Sci. U.S.A. (1992) 89: 3576-3580).

Another method that may be used is to direct mutagenesis to CDRs of  $V_H$  or  $V_L$  genes. Such techniques are disclosed by Barbas et al. (Proc. Nat. Acad. Sci. U.S.A. (1994) 91: 3809-3813) and Schier et al. (J. Mol. Biol. (1996) 263: 551-567).

Similarly, one or more, or all three CDRs may be grafted into a repertoire of  $V_H$  or  $V_L$  domains, which are then screened for an antigen-binding fragment specific for P2X4.

A portion of an immunoglobulin variable domain will comprise at least one of the CDRs substantially as set out herein and, optionally, intervening framework regions from the scFv fragments as set out herein. The portion may include at least about 50% of either or both of FR1 and FR4, the 50% being the C-terminal 50% of FR1 and the N-terminal 50% of FR4. Additional residues at the N-terminal or C-terminal end of the substantial part of the variable domain may be those not normally associated with naturally occurring variable domain regions. For example, construction of antibodies by recombinant DNA techniques may result in the introduction of N- or C-terminal residues encoded by linkers introduced to facilitate cloning or other manipulation steps. Other manipulation steps include the introduction of linkers to join variable domains to further protein sequences including immunoglobulin heavy chain constant regions, other variable domains (for example, in the production of diabodies), or proteinaceous labels as discussed in further detail below.

Although the embodiments illustrated in the Examples comprise a "matching" pair of  $V_H$  and  $V_L$  domains, a skilled artisan will recognize that alternative embodiments may comprise antigen-binding fragments containing only a single CDR from either  $V_L$  or  $V_H$  domain. In particular embodiments, the antigen-binding fragment is CDR3 of  $V_H$  (H3). Either one of the single chain specific binding domains can be used to screen for complementary domains capable of forming a two-domain specific antigen-binding fragment capable of, for example, binding to P2X4. The screening may be accomplished by phage display screening methods using the so-

called hierarchical dual combinatorial approach disclosed in WO92/01047, in which an individual colony containing either an H or L chain clone is used to infect a complete library of clones encoding the other chain (L or H) and the resulting two-chain specific binding domain is selected in accordance with phage display techniques as described.

5           Anti-P2X4 antibodies described herein can be linked to another functional molecule, e.g., another peptide or protein (albumin, another antibody, etc.). For example, the antibodies can be linked by chemical cross-linking or by recombinant methods.

10           The disclosed antibodies may also be altered to have a glycosylation pattern that differs from the native pattern. For example, one or more carbohydrate moieties can be deleted and/or one or more glycosylation sites added to the original antibody. Addition of glycosylation sites to the presently disclosed antibodies may be accomplished by altering the amino acid sequence to contain glycosylation site consensus sequences known in the art. Another means of increasing the number of carbohydrate moieties on the antibodies is by chemical or enzymatic coupling of glycosides to the amino acid residues of the antibody. Such methods are described in WO  
15           87/05330 and in Aplin et al. (1981) CRC Crit. Rev. Biochem., 22: 259-306. Removal of any carbohydrate moieties from the antibodies may be accomplished chemically or enzymatically, for example, as described by Hakimuddin et al. (1987) Arch. Biochem. Biophys., 259: 52; and Edge et al. (1981) Anal. Biochem., 118: 131 and by Thotakura et al. (1987) Meth. Enzymol., 138: 350. The antibodies may also be tagged with a detectable, or functional, label. Detectable  
20           labels include radiolabels such as <sup>131</sup>I or <sup>99</sup>Tc, which may also be attached to antibodies using conventional chemistry. Detectable labels also include enzyme labels such as horseradish peroxidase or alkaline phosphatase. Detectable labels further include chemical moieties such as biotin, which may be detected via binding to a specific cognate detectable moiety, e.g., labeled avidin.

25           Typically, an amino acid is substituted by a related amino acid having similar charge, hydrophobic, or stereochemical characteristics. Such substitutions would be within the ordinary skills of an artisan. Unlike in CDRs, more substantial changes can be made in FRs without adversely affecting the binding properties of an antibody. Changes to FRs include, but are not limited to, humanizing a non-human derived or engineering certain framework residues that are  
30           important for antigen contact or for stabilizing the binding site, e.g., changing the class or subclass of the constant region, changing specific amino acid residues which might alter the

effector function such as Fc receptor binding, e.g., as described in U.S. Pat. Nos. 5,624,821 and 5,648,260 and Lund et al. (1991) J. Immun. 147: 2657-2662 and Morgan et al. (1995) Immunology 86: 319-324, or changing the species from which the constant region is derived.

One of skill in the art will appreciate that the modifications described above are not all-  
5 exhaustive, and that many other modifications would be obvious to a skilled artisan in light of the teachings of the present disclosure.

### **Nucleic Acids, Cloning and Expression Systems**

The present disclosure provides the amino acid sequence of the disclosed antibodies.

10 Once provided with this information, one of skill in the art could readily obtain nucleic acid molecules encoding the disclosed antibodies. The nucleic acids may comprise DNA or RNA and may be wholly or partially synthetic or recombinant. Reference to a nucleotide sequence encompasses a DNA molecule with the specified sequence, and encompasses a RNA molecule with the specified sequence in which U is substituted for T, unless context requires otherwise.

15 The nucleic acids molecules of the invention comprise a coding sequence for a CDR, a V<sub>H</sub> domain, and/or a V<sub>L</sub> domain disclosed herein.

The present disclosure also provides constructs in the form of plasmids, vectors, phagemids, transcription or expression cassettes which comprise at least one nucleic acid molecule encoding a CDR, a V<sub>H</sub> domain, and/or a V<sub>L</sub> domain disclosed herein.

20 The disclosure further provides a host cell which comprises one or more constructs as above.

Also provided are nucleic acids encoding any CDR (H1, H2, H3, L1, L2, or L3), V<sub>H</sub> or V<sub>L</sub> domain, as well as methods of making of the encoded products. The method comprises expressing the encoded product from the encoding nucleic acid. Expression may be achieved by  
25 culturing under appropriate conditions recombinant host cells containing the nucleic acid. Following production by expression a V<sub>H</sub> or V<sub>L</sub> domain, or specific binding member may be isolated and/or purified using any suitable technique, then used as appropriate.

Antigen-binding fragments, V<sub>H</sub> and/or V<sub>L</sub> domains and encoding nucleic acid molecules and vectors may be isolated and/or purified from their natural environment, in substantially pure  
30 or homogeneous form, or, in the case of nucleic acid, free or substantially free of nucleic acid or genes of origin other than the sequence encoding a polypeptide with the required function.

Systems for cloning and expression of a polypeptide in a variety of different host cells are well known in the art. For cells suitable for producing antibodies, see *Gene Expression Systems*, Academic Press, eds. Fernandez et al., 1999. Briefly, suitable host cells include bacteria, plant cells, mammalian cells, and yeast and baculovirus systems. Mammalian cell lines available in the art for expression of a heterologous polypeptide include Chinese hamster ovary cells, HeLa cells, baby hamster kidney cells, NS0 mouse myeloma cells, and many others. A common bacterial host is *E. coli*. Any protein expression system compatible with the invention may be used to produce the disclosed antibodies. Suitable expression systems include transgenic animals described in *Gene Expression Systems*, Academic Press, eds. Fernandez et al., 1999.

Suitable vectors can be chosen or constructed, so that they contain appropriate regulatory sequences, including promoter sequences, terminator sequences, polyadenylation sequences, enhancer sequences, marker genes and other sequences as appropriate. Vectors may be plasmids or viral, e.g., phage, or phagemid, as appropriate. For further details see, for example, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, 1989. Many known techniques and protocols for manipulation of nucleic acid, for example, in preparation of nucleic acid constructs, mutagenesis, sequencing, introduction of DNA into cells and gene expression, and analysis of proteins, are described in detail in *Current Protocols in Molecular Biology*, 2nd Edition, eds. Ausubel et al., John Wiley & Sons, 1992.

A further aspect of the disclosure provides a host cell comprising a nucleic acid as disclosed here. A still further aspect provides a method comprising introducing such nucleic acid into a host cell. The introduction may employ any available technique. For eukaryotic cells, suitable techniques may include calcium phosphate transfection, DEAE-Dextran, electroporation, liposome-mediated transfection and transduction using retrovirus or other virus, e.g., vaccinia or, for insect cells, baculovirus. For bacterial cells, suitable techniques may include calcium chloride transformation, electroporation and transfection using bacteriophage. The introduction of the nucleic acid into the cells may be followed by causing or allowing expression from the nucleic acid, e.g., by culturing host cells under conditions for expression of the gene.

## Methods of Use

The disclosed anti-P2X4 antibodies are capable of modulating the electrophysiological activity of P2X4. In particular, antibodies provided herein may be used to inhibit or potentiate P2X4 channel conductance. Such antibodies can be used to treat P2X4-associated medical disorders in mammals, especially, in humans. In particular, antibodies that inhibit P2X4 activity are useful for the treatment of neuropathic pain. Antibodies that potentiate P2X4 activity are useful in other therapeutic methods, including but not limited to microglia-mediated diseases and disorders and macrophage-mediated diseases and disorders.

Antibodies of the invention can also be used for isolating P2X4 or P2X4-expressing cells.

As demonstrated in the Examples, binding of P2X4 with an anti-P2X4 antibody modulates P2X4 biological activity by potentiating or reducing passage of ions through the P2X4 channel.

The antibodies or antibody compositions of the present invention are administered in therapeutically effective amounts. Generally, a therapeutically effective amount may vary with the subject's age, condition, and sex, as well as the severity of the medical condition of the subject. The appropriate dose is chosen based on clinical indications by a treating physician.

The antibodies may be given as a bolus dose, to maximize the circulating levels of antibodies for the greatest length of time after the dose. Continuous infusion may also be used after the bolus dose.

Anti- P2X4 antibodies of the invention may be used to detect the presence of P2X4 in biological samples. Detection methods that employ antibodies are well known in the art and include, for example, ELISA, radioimmunoassay, immunoblot, Western blot, immunofluorescence, and immunoprecipitation. If desired, an anti-P2X4 antibody is modified, for example, with a ligand group (such as biotin) or a detectable marker group (such as a fluorescent group, a radioisotope or an enzyme). If desired, the antibodies of the invention may be labeled using conventional techniques. Suitable detectable labels include, for example, fluorophores, chromophores, radioactive atoms, electron-dense reagents, enzymes, and ligands having specific binding partners. Enzymes are typically detected by their activity. For example, horseradish peroxidase can be detected by its ability to convert tetramethylbenzidine (TMB) to a blue pigment, quantifiable with a spectrophotometer. For detection, suitable binding partners include, but are not limited to, biotin and avidin or streptavidin, IgG and protein A, and the

numerous receptor-ligand couples known in the art. Other permutations and possibilities will be readily apparent to those of ordinary skill in the art, and are considered as equivalents within the scope of the invention.

## 5 **Pharmaceutical Compositions and Methods of Administration**

The invention provides pharmaceutical compositions comprising anti-P2X4 antibodies (e.g., Antibody Nos. 1-48). Such compositions are likely suitable for pharmaceutical use and administration to patients. The compositions typically comprise one or more antibodies of the present invention and a pharmaceutically acceptable excipient. The phrase “pharmaceutically acceptable excipient” includes any and all solvents, dispersion media, coatings, antibacterial agents and antifungal agents, isotonic agents, and absorption delaying agents, and the like, that are compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. The compositions may also contain other active compounds providing supplemental, additional, or enhanced therapeutic functions.

15 The pharmaceutical compositions may also be included in a container, pack, or dispenser together with instructions for administration.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Methods to accomplish the administration are known to those of ordinary skill in the art. The administration may, for example, be intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous or transdermal. In one embodiment, neuropathic pain is treated by intrathecal administration. It may also be possible to obtain compositions which may be topically or orally administered, or which may be capable of transmission across mucous membranes.

Solutions or suspensions used for intradermal or subcutaneous application typically include one or more of the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerin, propylene glycol, or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates; and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric

25

30

acid or sodium hydroxide. Such preparations may be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injection include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi.

Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars; polyalcohols such as mannitol, sorbitol, and sodium chloride in the composition. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or by the use of surfactants. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate, and gelatin.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For oral administration, the antibodies can be combined with excipients and used in the form of tablets, troches, or capsules.

Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches, and the like can contain any of the following ingredients, or compounds of a similar nature; a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration may be accomplished, for example, through the use of lozenges, nasal sprays, inhalers, or suppositories. For example, in case of antibodies that comprise the Fc portion, compositions may be capable of transmission across mucous membranes in intestine, mouth, or lungs (e.g., via the FcRn receptor-mediated pathway as described in U.S. Pat. No. 6,030,613). For transdermal administration, the active compounds may be formulated into ointments, salves, gels, or creams as generally known in the art. For administration by inhalation, the antibodies may be delivered in the form of an aerosol spray from pressured container or dispenser, which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

In certain embodiments, the presently disclosed antibodies are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. Liposomal suspensions containing the presently disclosed antibodies can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Pat. No. 4,522,811.

It may be advantageous to formulate oral or parenteral compositions in a dosage unit form for ease of administration and uniformity of dosage. The term "dosage unit form" as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

Toxicity and therapeutic efficacy of the composition of the invention can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD<sub>50</sub> (the dose lethal to 50% of the population) and the ED<sub>50</sub> (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic

effects is the therapeutic index and it can be expressed as the ratio  $LD_{50}/ED_{50}$ . Compositions that exhibit large therapeutic indices are preferred.

The data obtained from electrophysiological experiments and animal studies can be used in formulating a range of dosage for use in humans. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the  $IC_{50}$  (i.e., the concentration of the antibody which achieves a half-maximal inhibition of symptoms). Circulating levels in plasma may be measured, for example, by high performance liquid chromatography. The effects of any particular dosage can be monitored by a suitable bioassay. The dosage lies preferably within a range of circulating concentrations with little or no toxicity. The dosage may vary depending upon the dosage form employed and the route of administration utilized.

### Kits

The invention provides kits for modulating P2X4 activity. Antibodies that potentiate P2X4 activity are useful for the treatment of indications mediated by decreased P2X4 activity as described herein. Antibodies that inhibit P2X4 activity are useful for the treatment or prevention of neuropathic pain and/or microglia-mediated diseases and disorders and/or macrophage-mediated diseases and disorders. In one embodiment, the kit includes a therapeutic or prophylactic composition containing an effective amount of an anti-P2X4 antibody that modulates P2X4 activity in unit dosage form.

In some embodiments, the kit comprises a sterile container which contains a therapeutic or prophylactic cellular composition; such containers can be boxes, ampules, bottles, vials, tubes, bags, pouches, blister-packs, or other suitable container forms known in the art. Such containers can be made of plastic, glass, laminated paper, metal foil, or other materials suitable for holding medicaments.

If desired an antibody of the invention is provided together with instructions for administering the antibody or agent to a subject having or at risk of developing neuropathic pain. The instructions will generally include information about the use of the composition for the treatment or prevention of such indications. In other embodiments, the instructions include at least one of the following: description of the therapeutic agent; dosage schedule and administration for treatment or prevention of an immune disorder or symptoms thereof; precautions; warnings; indications; counter-indications; overdose information; adverse

reactions; animal pharmacology; clinical studies; and/or references. The instructions may be printed directly on the container (when present), or as a label applied to the container, or as a separate sheet, pamphlet, card, or folder supplied in or with the container.

The practice of the present invention employs, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, biochemistry and immunology, which are well within the purview of the skilled artisan. Such techniques are explained fully in the literature, such as, "Molecular Cloning: A Laboratory Manual", second edition (Sambrook, 1989); "Oligonucleotide Synthesis" (Gait, 1984); "Animal Cell Culture" (Freshney, 1987); "Methods in Enzymology" "Handbook of Experimental Immunology" (Weir, 1996); "Gene Transfer Vectors for Mammalian Cells" (Miller and Calos, 1987); "Current Protocols in Molecular Biology" (Ausubel, 1987); "PCR: The Polymerase Chain Reaction", (Mullis, 1994); "Current Protocols in Immunology" (Coligan, 1991). These techniques are applicable to the production of the polynucleotides and polypeptides of the invention, and, as such, may be considered in making and practicing the invention. Particularly useful techniques for particular embodiments will be discussed in the sections that follow.

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the anti-P2X4 antibodies in assay, screening, and therapeutic methods of the invention, and are not intended to limit the scope of what the inventors regard as their invention.

## EXAMPLES

### Example 1: Production and isolation of recombinant P2X4 proteins

Human P2X purinoceptor 4 (Q99571), a natural variant of human P2X purinoceptor 4 with an S to G mutation at position 242 (Corresponds to variant rs25644) and murine P2X purinoceptor 4 (Q9JJX6) proteins were designed with a C-terminal AVI tag (Avidity LLC) and a C-terminal Histidine tag. The constructs were cloned into pFASTBAC1 vectors (Life Technologies). Bacmids were generated in DH10Bac (Life Technologies) *E. coli* cells. Bacmids were subsequently transfected into Sf9 insect cells (*Spodoptera frugiperda* Sf9 cells from Life

Technologies, cat no 11496-015) for production of recombinant baculovirus particles, which in turn were used to infect Sf9 cells for protein expression.

Expression parameters were assessed by monitoring expression level, protein quality and the homogeneity of the receptor using a modified Fluorescence-detection size-exclusion chromatography (FSEC) method described by Backmark et al., (Protein Sci. 22 (2013) 1124-1132). This method is similar to the basic FSEC concept as described by Kawate and Gouaux (Structure 14 (2006) 673-681), but applied a fluorescent probe that specifically interacts with the Histidine tag on the protein. Cells were typically inoculated at a density of  $1.0 \times 10^6$ /mL in SF900II medium. Cells were infected with a multiplicity of infection of 2 at a cell density of  $2 \times 10^6$  cells/ml. Protein expression was performed at 27°C and cells were harvested 72 hours post infection. Expression parameters were selected to enhance the quantity of trimer and homogeneity of protein present as trimers. As assayed by fluorescent size exclusion chromatography, the protein preparation contains 50-75% trimer. Although the total amount of receptor increased with longer post infection times, FSEC analysis indicated that protein quality declined when the expression time was increased past 72 hours.

Human P2X4 receptor and mouse P2X4 were purified as follows. Membranes were prepared from SF9 cells. Membrane proteins were extracted from the membranes by detergent solubilization, using combinations of detergents, salts, buffers and additives, including n-Dodecyl-beta-D-Maltoside CAS 69227-93-6 (0-2% (w/v)), n-Dodecyl thio-Maltoside CAS 148565-58-6 (0-1% (w/v)), (3-[(3-Cholamidopropyl)-Dimethylammonio]-1-Propane Sulfonate/N,N-Dimethyl-3-Sulfo-N-[3-[[3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ]-3,7,12-Trihydroxy-24-Oxocholan-24-yl]Amino]propyl]-1-Propanaminium Hydroxide abbreviated to CHAPS CAS 75621-03-3 (0-0.6% (w/v)), and Cholesteryl Hemisuccinate CAS 102601-49-0 (0-0.12% (w/v)). Without being bound to theory, higher concentrations of the indicated substances as well as alternative detergents support extraction of the protein from the membranes. The proteins underwent standard affinity and size exclusion chromatography purification. The purified protein was formulated in a buffer which contained 50 mM Tris-HCl pH 8.0, 600 mM NaCl, 10% (v/v) glycerol, 0.025 (w/v) % n-Dodecyl-beta-D-Maltoside CAS 69227-93-6, 0.0125% (w/v) , n-Dodecyl thio-Maltoside CAS 148565-58-6, 0.0075% (w/v) (3-[(3-Cholamidopropyl)-Dimethylammonio]-1-Propane Sulfonate/N,N-Dimethyl-3-Sulfo-N-[3-[[3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ]-3,7,12-

Trihydroxy-24-Oxocholan-24-yl]Amino]propyl]-1-Propanaminium Hydroxide abbreviated to CHAPS CAS 75621-03-3, and 0.0015% (w/v) Cholesteryl Hemisuccinate CAS 102601-49-0.

The purified protein was formulated under alternative conditions, including phosphate buffers and HEPES buffers 2-[4-(2-hydroxyethyl)piperazin-1-yl]ethanesulfonic acid buffers

5 CAS 7365-45-9. The pH of the various buffers has ranged from 7.0-8.0. Salt (NaCl) has been varied between 120-600 mM. Glycerol can be excluded from the protein formulation. Various detergents have been used in protein formulation, such as lauryl maltose neopentyl glycol 2,2-didecylpropane-1,3-bis- $\beta$ -D-maltopyranoside, decyl maltose neopentyl glycol 2,2-

dioctylpropane-1,3-bis- $\beta$ -D-maltopyranoside, octyl maltose neopentyl glycol 2,2-

10 dihexylpropane-1,3-bis- $\beta$ -D-maltopyranoside, CYMAL-5 5-Cyclohexyl-1-pentyl- $\beta$ -D-maltoside

CAS 250692-65-0, n-Tetradecylphosphocholine 77733-28-9, n-Decyl- $\beta$ -D-Maltopyranoside

CAS 82494-09-5, n-octyl- $\beta$ -D-glucoside CAS 29836-26-8 and n-nonyl- $\beta$ -D-glucoside CAS

69984-73-2. Formulations in other detergents are also possible. The concentration of Cholesteryl

Hemisuccinate CAS 102601-49-0 can be varied and excluded from the protein formulation as

15 well.

### Example 2: Purification of Trimeric P2X4 complexes

*In vivo*, P2X receptors form functional trimeric ion channels. The solubilised and purified P2X4 proteins are typically present in a range of oligomeric states, including monomers, dimers,

20 trimers, and hexamers (i.e., dimers of trimers). This range of oligomeric states is described for

example, by references (Backmark et al., Protein Sci. 22 (2013) 1124-1132; Kawate et al.,

Structure 14 (2006) 673-681; Kawate et al., Nature 460 (2009) 592-598; Nakazawa et al.,

European Journal of Pharmacology 518 (2005) 107-110; Nicke et al., Mol. Pharmacol. 63 (2003)

243-252). To obtain a stable predominantly trimeric arrangement, solubilization conditions were

25 adjusted.

Combinations of detergents, additives, buffers and pH were varied. Optimal conditions were selected to increase the FSEC signature of the trimer while reducing larger order oligomeric arrangements and aggregates. Such undesirable forms were eluted in the void volume of the size-

exclusion columns applied. Conditions tested included KPO<sub>4</sub>-HCl pH 7.4, 600 mM NaCl and

30 2% (w/v) n-dodecyl-beta-maltopyranoside CAS 69227-93-6. Optimal solubilization was

obtained in buffers containing combinations of the detergents including n-Dodecyl-beta-D-

Maltoside CAS 69227-93-6, n-Dodecyl thio-Maltoside CAS 148565-58-6, (3-[(3-Cholamidopropyl)-Dimethylammonio]-1-Propane Sulfonate/N,N-Dimethyl-3-Sulfo-N-[3-[[3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-Trihydroxy-24-Oxocholan-24-yl]Amino]propyl]-1-Propanaminium Hydroxide abbreviated to CHAPS CAS 75621-03-3, and the additive Cholesteryl Hemisuccinate CAS 102601-49-0. The purified protein was formulated in a buffer which contained 50 mM Tris-HCl pH 8.0, 600 mM NaCl, 10% (v/v) glycerol, 0.025 (w/v) % n-Dodecyl-beta-D-Maltoside CAS 69227-93-6, 0.0125% (w/v) , n-Dodecyl thio-Maltoside CAS 148565-58-6, 0.0075% (w/v) (3-[(3-Cholamidopropyl)-Dimethylammonio]-1-Propane Sulfonate/N,N-Dimethyl-3-Sulfo-N-[3-[[3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-Trihydroxy-24-Oxocholan-24-yl]Amino]propyl]-1-Propanaminium Hydroxide abbreviated to CHAPS CAS 75621-03-3, and 0.0015% (w/v) Cholesteryl Hemisuccinate CAS 102601-49-0.

**Example 3: Anti-P2X4 specific antibodies were isolated using phage display selection.**

Naïve human single chain Fv (scFv) phage display libraries were cloned into a phagemid vector based on the filamentous phage M13 were used for selections (Lloyd (2009) Protein Eng Des Sel 22, 159-168; Vaughan et al., Nature biotechnology 14, 309-314, 1996). Anti-P2X4 specific antibodies were isolated from the phage display libraries using a series of selection cycles on recombinant human P2X4 (hu P2X4), essentially as previously described by Vaughan et al (Vaughan et al., supra). In brief, human P2X4 in PBS (Dulbecco's PBS, pH7.4) was immobilised onto wells of a MaxiSorp® microtitre plate (Nunc) overnight at 4°C. Wells were washed with PBS then blocked for 1 hour with PBS-Marvel dried skimmed milk (3% w/v). Purified phage in PBS-Marvel (3% w/v) were added to the wells and allowed to bind coated antigen for 1 hour at room temperature. Unbound phage was removed by a series of wash cycles using PBS. Bound phage particles were eluted with trypsin for 30 minutes at 37°C, infected into *E.coli* TG1 bacteria and rescued for the next round of selection. Alternatively, anti-P2X4 antibodies were isolated as described above except deselection of the purified phage library against the C-terminal peptide huP2X4<sub>370-388</sub> (Alomone Labs #APR-002) or phenyl hydrophobic interaction chromatography (HIC) beads was performed prior to selection with the antigen.

**Example 4: Generation of rat anti-murine P2X4 antibodies using hybridoma technology.**

***Immunisations***

Purified recombinant murine P2X4 protein and murine P2X4 transfected HEK 293F cells were used to immunise Sprague Dawley rats in three groups. For group 1, rats were immunised with murine P2X4 protein; for group 2, rats were immunised with murine P2X4 transfected HEK 293F cells; and for group 3, rats were immunised by alternating murine P2X4 protein and murine P2X4 transfected HEK 293F cells.

A twenty eight day immunization protocol was used with a priming immunization on day 0, followed by four subsequent booster immunizations on days 7, 15, 22 and 24. For group 1, equal volumes of complete Freund's adjuvant and murine P2X4 protein (total protein: 100 µg) were emulsified together, and delivered to the rats subcutaneously at two sites (200 µL per site). For the subsequent three booster injections, the same amount of protein was used, emulsified in Freund's incomplete adjuvant. For group 2, murine P2X4 transfected HEK 293F cells were resuspended at 5E7 cells per mL in PBS and emulsified with equal volumes of complete Freund's adjuvant. As above, the cells were injected into rats at two sites (200 µL per site). For the subsequent three booster injections, the same number of cells was used, emulsified in Freund's incomplete adjuvant. For group 3, the priming immunization was with murine P2X4 protein as per group 1 above, followed by three booster immunizations with murine P2X4 transfected HEK 293F cells, murine P2X4 protein, and murine P2X4 transfected HEK 293F cells.

The final boosts were given intraperitoneally on day 24, group 1 and group 3 rats received murine P2X4 protein (400 µL at 50 µg/mL in Tris buffer), and group 2 rats received murine transfected HEK 293F cells (400 µL at 5E7/mL).

Tail vein bleeds were obtained from the rats before immunisation, on day 13 after the first immunization, and on day 20 after second immunisation. The IgG titres to anti-murine P2X4 were determined by a cell-based DELFIA (dissociation-enhanced lanthanide fluorescence immunoassay) assay.

#### ***Assessment of rat immune response to murine P2X4 using a cell-based DELFIA***

The IgG titres to murine P2X4 in sera were determined by a cell based DELFIA using both mP2X4 transfected HEK 293F and parental HEK cells. In order to reduce anti-HEK 293F cell specific antibodies in sera, before being assayed the serum samples from rats immunised with either cells alone or the alternating protein and cells strategy were incubated with non-

transfected HEK 293F cells. The sera from rats immunised with protein were assayed without this pre-adsorption step.

Murine P2X4 transfected HEK 293F and parental HEK cells were plated in culture media onto black collagen coated 96 well microtitre plates at a density of 30,000 cells per well. After overnight incubation at 37°C in a 5% CO<sub>2</sub> incubator, the culture supernatant was removed and the cells were fixed with 3.7% formaldehyde solution at 50 µL per well. All subsequent incubations were carried out at room temperature. After 5 minutes fixation, the formaldehyde solution was discarded and replaced with 200 µL of 3% marvel/PBS blocking buffer. After one hour, the blocking buffer was removed and the serum samples added in a 3-fold dilution series (50 µL per well starting from a 1:200 dilution). After incubating for one hour, the wells were washed gently three times with PBS supplemented with 0.05% (v/v) Tween 20. A biotinylated polyclonal goat anti-rat IgG Fc gamma specific secondary antibody (diluted 1:500 in marvel/PBS) was added then at 50 µL per well. Following a further one hour incubation and three gentle washes as above, Eu-N1-labeled streptavidin (Perkin Elmer) was added to the wells (diluted to 100 ng/mL in marvel/PBS, 50 µL per well). After 30 minutes incubation time, the wells were gently washed five times and DELFIA enhancement solution was added. The reaction was allowed to develop for 10 minutes, and then the plate was then read using a PerkinElmer EnVision 2103 multilabel plate reader. The TRF (time-resolved fluorescence) signal in each well was measured (excitation 340 nm, emission 615 nm).

The serum titration curves for murine P2X4 transfected HEK 293F cells and parental HEK 293F cells were plotted and the respective area under the curves (AUC) calculated. For rats immunized with murine P2X4 transfected HEK 293F cells, specific mP2X4 IgG titres were derived by subtracting the AUC values from parental HEK cells from the AUC values for the murine P2X4 transfected cells.

### ***Monoclonal rat IgG isolation***

Four days after the final boost, lymph nodes were aseptically harvested and cells were isolated by mechanical disruption and counted. These cells were mixed with SP2/0 myeloma cells and fused using an electrofusion apparatus. The resultant fusions were mixed with a methylcellulose-based semi-solid media and plated out into OmniTray plates. The semi-solid media comprised CloneMatrix and DMEM supplemented with 20% FCS, 10% BM Condimed

H1, 1mM sodium pyruvate and OPI media supplement, 2% hypoxanthine azaserine and FITC conjugated goat anti-rat IgG. The cells in semi-solid media were cultured for 13 days at 37°C in a 5% CO<sub>2</sub> incubator. During this incubation period, clonal colonies are formed from a single progenitor hybridoma cell. These colonies secrete IgG that is trapped in the vicinity of the colony by the FITC conjugated anti-IgG present in the semi-solid media. The resultant immune complex formation can be observed around the cell as a fluorescent 'halo' when visualised by ClonePix FL colony picker (Molecular Devices). These haloed colonies are then picked into 96 well microtitre plates.

After 3-5 days in culture, the supernatants of the picked colonies were harvested and screened for murine P2X4 specificity by comparing binding to murine P2X4 transfected HEK 293F cells and parental HEK 293F cells by a cell-based fluorometric microvolume assay technology (FMAT) assay.

#### ***DNA sequencing of rat IgG***

Messenger RNA (mRNA) was extracted from cells using magnetic oligo (dT) particles and converted into cDNA. PCR amplification was performed using poly-C and constant region VH/VL primers.

#### ***Rat IgG purifications***

Prior to purification, the hybridomas were tested by ELISA using a goat anti-rat IgG2a coated microtitre plate to determine which clones secreted Rat IgG2a, as this isotype is purified using a different purification matrix to rat IgG1, IgG2b and IgG2c isotypes.

Cells were propagated in 24 well plates and overgrown in serum free HL-1 medium supplemented with HyperZero and glutamine. After 10 days, the supernatants were transferred to 96 well masterblocks and rat IgG1, IgG2b and IgG2c isotypes were purified on 20µL Phytips containing ProPlus resin (Phynexus). Rat IgG2a antibodies were purified on custom packed Phytips containing CaptureSelect IgG-Fc multiple species resin (Lift Technologies) using Perkin Elmer Minitrack. The captured rat IgGs were eluted with 75µL of 100 mM HEPES, 140 mM NaCl pH 3.0 then neutralised with an equal volume of 200 mM HEPES pH 8.0. The purified IgGs were quantified using an absorbance reading at 280 nm in UV-Star 384 well plate.

### ***Reformatting of rat IgGs to human IgG1***

Rat hybridoma IgG clones were molecularly reformatted to generate chimeric constructs expressing rat VH and VL domains and human IgG1 constant domains essentially as described by Persic et al., 1997 (Gene 187, 9-18) with the following modifications. An OriP fragment was included in the expression vectors to facilitate use with CHO-transient cells and to allow episomal replication. The VH domain was cloned into a vector (pEU1.4) containing the human heavy chain constant domains and regulatory elements to express whole IgG1 heavy chain in mammalian cells. This constant region contained the triple mutations (TM) L234F/L235E/P331S resulting in an effector null human IgG1 (Oganesyan et al., (2008) Acta Crystallogr D Biol Crystallogr. 64, 700-704). Similarly, the VL domain was cloned into a vector (pEU4.4) for the expression of the human light chain (lambda) constant domains and regulatory elements to express whole IgG light chain in mammalian cells. To obtain IgGs, the heavy and light chain IgG expressing vectors were transfected into CHO-transient mammalian cells. IgGs were expressed and secreted into the medium. Harvests were filtered prior to purification, then IgG was purified using Protein A chromatography. Culture supernatants were loaded on a column of appropriate size of Ceramic Protein A (Pall 20078-036) and washed with 50 mM Tris-HCl pH 8.0, 250 mM NaCl. Bound IgG was eluted from the column using 0.1 M Sodium Citrate (pH 3.0) and neutralised by the addition of Tris-HCl (pH 9.0). The eluted material was buffer exchanged into PBS using Nap10 columns (GE Lifesciences 17-0854-02) and the concentration of IgG was determined spectrophotometrically using an extinction coefficient based on the amino acid sequence of the IgG (Pace et al., (1995) Protein Sci. 4, 2411-23). The purified IgG were analysed for purity using SDS-PAGE.

### **Example 5: Identification of human P2X4 binding antibodies from phage display selections.**

ScFv antibodies identified from the phage display method described in Example 3 were expressed in bacteria and screened as unpurified bacterial periplasmic extracts (which contain scFv), prepared in: 0.2M HEPES buffer pH7.4, 0.5 mM EDTA and 0.5 M sucrose.

Alternatively, the heavy and light chain variable regions were amplified by PCR and cloned into a vector for expression as human IgG1 antibodies in HEK293F cells.

For screening of bacterial scFv samples, 5µl of bacterial extract was added to a 384 well assay plate (Corning 3655). Assay buffer was prepared as follows: 1X Hanks Balanced Salt Solution (HBSS) (Sigma H8264), 0.1% (v/v) BSA (PAA K05-013), 20mM HEPES (Gibco 15630) and 1U/ml Apyrase (Sigma A6535) and 5µl added to the assay plate with the bacterial scFv extract. Anti-myc detection reagent (Serotec MCA2200) and anti-mouse DyLight649 (Jackson Immuno Research Labs 115-495-071) were diluted in assay buffer to 15.6nM and 24nM respectively in the same solution and 5µl added to the assay plate with the scFv sample.

HEK293F cells expressing human P2X4 (huP2X4) (Q99571, ENSP00000336607) were diluted to  $2.6 \times 10^5$  cells/ml in assay buffer and 15µl added to the assay plate. In parallel scFv samples were also tested for binding to HEK293F cells that did not express huP2X4.

For screening of the HEK293F expressed IgG samples, 2.5µl of cell culture supernatant was added to the 384 well assay plate (Corning 3655). Assay buffer was prepared as described above and 7.5µl was added to the assay plate with the IgG sample. Anti-human AlexaFluor 647 (Life Technologies A21445) was diluted in assay buffer to 6nM and 10µl added to the assay plate with the IgG sample. HEK293F cells expressing huP2X4 (Q99571, ENSP00000336607) were diluted to  $4 \times 10^5$  cells/ml in assay buffer and 10µl added to the assay plate. In parallel IgG samples were also tested for binding to HEK293F cells that did not express huP2X4. Assay plates set up to screen both types of samples were sealed with a Topseal plate sealer (Perkin Elmer 6005250) and incubated at room temperature for at least 4hours before reading on the Fluorescence Microvolume Assay Technology (FMAT), a fluorescence based platform that detects fluorescence localized to bead or cells settled at the bottom of a microwell (Dietz et al., Cytometry 23:177-186 (1996), Miraglia et al., J. Biomol. Screening 4:193-204 (1999)). Data was analysed using the FMAT analysis software and events were gated based on fluorescence 0-10,000 FL1 counts, colour typically 0.15 to 0.40 and size 10-60. A minimum count of 20 events was set as a threshold before data was reported for each well. ScFv showing binding to the HEK293F huP2X4 cells, but not to the control HEK293F cells were selected for further testing if the FL1 count was above 1000 on the huP2X4 cells, IgG samples showing a specific huP2X4 binding signal of greater than 200 FL1 counts were identified as hits and characterised further.

ScFv or IgG samples which showed a specific binding signal to HEK293F huP2X4 cells as unpurified samples were subjected to DNA sequencing (Vaughan et al. supra, Nature Biotechnology 14: 309-314), (Osborn 1996; Immunotechnology. 2, 181-196). Unique scFvs were expressed in bacteria and purified by affinity chromatography (as described by Bannister et al (2006) Biotechnology and bioengineering, 94. 931-937). Those scFv that confirmed binding to human P2X4 were generated as full IgGs and expressed and purified as described in Example 4. Purified IgG antibodies were tested for functional activity in the electrophysiology assay and for binding to cells expressing mouse and cynomolgus P2X4 using the same method described for the human P2X4 cells described above except a titration of purified IgG sample was used. Results of electrophysiology assays are provided at Figures 3 and 4.

#### **Example 6: Identification of hybridoma IgGs that bind specifically to murine P2X4**

Supernatants generated from the immunisations were screened to identify IgGs with specific binding to mP2X4. Briefly supernatants were diluted 10 fold into assay buffer (HBSS, 0.1% (v/v) BSA, 20mM HEPES and 1U/ml Apyrase) and 5µl added to the assay plate. Anti-rat detection antibody labeled with Alexa Fluor 647 (Jackson Immuno Research labs) was diluted to 6nM and 10µl added to the assay plate. HEK293F cells expressing mP2X4 were diluted to  $2.6 \times 10^5$ /ml and 15µl added to the assay plate. IgG samples were also tested for non-specific binding in parallel by testing the samples for binding to HEK293F cells. IgGs demonstrating specific binding to mP2X4 and no binding to HEK293F cells were identified as hits and selected for antibody purification and analysis by electrophysiology. Results of the electrophysiology screen are provided in Figure 7 together with the binding results for these samples against human and cyno P2X4 expressing cell lines using the same assay described previously

#### **Example 7: Generation of human P2X4 variants and expression by transient transfection in HEK293F cells**

To determine the epitope to which the P2X4 functional antibodies bind the following mutations were generated in human P2X4; E95Q, V105M, G114D, A122V, S131N, A151P, G154R, L303P, N306K. DNA vectors containing huP2X4 sequences with these changes were generated using standard molecular biology techniques. DNA vectors were transfected into HEK293F cells using 293-fectin (Life Technologies 12347019) following the manufacturers

guidelines. Cells expressing the huP2X4 variants were incubated with Antibody Nos. 1, 11, 29, and 33 together with the anti-human AlexaFluor 647 (Life Technologies A21445) detection reagent. Binding was measured using the FMAT plate reader. Variant S131N was shown to be important for the binding of Antibody Nos. 11, 29, and 33. Figures 1A-1D show the results of FMAT assays characterizing binding of P2X4 antibodies to HEK293F cells expressing variants of human P2X4.

#### **Example 8: Electrophysiological characterization of monoclonal antibodies to P2X4.**

##### ***Methods for phage display derived mAbs:- Figures 3 & 4***

HEK 293F cells stably expressing human P2X4, mouse P2X4 or cynomolgus P2X4 were harvested at 50% confluency using accutase. Cells were then resuspended in 10 ml Freestyle 293F media supplemented with HEPES (10 mM) + apyrase (1U/ml, ATPase/ADPase activity = 1) at a density of  $2-3 \times 10^6$  cells/ml. P2X4 function was assayed using the automated electrophysiology platform QPatch 16X (Sophion) in population patch configuration. Composition of QPatch extracellular buffer (QEB) was (in mM) NaCl (140), KCl (2), MgCl<sub>2</sub> (1) CaCl<sub>2</sub> (2), HEPES (10). Final composition of compound plate extracellular buffer (CPEB1) was NaCl (137.6), KCl (2.2), MgCl<sub>2</sub> (0.66), CaCl<sub>2</sub> (1.3), HEPES (6.6), KH<sub>2</sub>PO<sub>4</sub> (0.49), NaH<sub>2</sub>PO<sub>4</sub> (2.66). pH of extracellular buffers was adjusted to 7.4 with NaOH (1 M), osmolarity was adjusted to 300 mOsm with sucrose and the solutions were 0.2  $\mu$ m filtered. Compound plate extracellular buffer was supplemented with 0.1% bovine serum albumin. The QPatch intracellular buffer contained (in mM) CsF (140), NaCl (10), EGTA (1), HEPES (10). pH of the intracellular buffer was adjusted to 7.3 with CsOH (1 M) and the solution was 0.2  $\mu$ m filtered. IgGs were titrated to pH 7.4 with NaOH (1 M).

After obtaining whole cell configuration, cells were voltage clamped at -50 mV with 70% series resistance compensation employed. The ligand agonist adenosine 5'-triphosphate disodium salt (ATP, 3  $\mu$ M) in CPEB1 was applied for 3 seconds every 5 minutes for 20 minutes resulting in 4 control agonist responses. Each agonist response was washed off with CPEB1 + apyrase (1U/ml). 4 additional agonist responses were then measured every 5 minutes in the continued presence of the test IgG or an isotype control IgG (NIP 228). Exemplar traces showing the effect of inhibitory IgGs 5 mins after IgG application can be seen in Figure 8A whereas an example of a potentiating IgG can be seen in Figure 8D. Electrophysiology data presented in

Figure 3 and Figure 4 were leak subtracted by subtracting the current in the absence of ligand and the magnitude of the P2X4 response measured as the peak inward current in the presence of ligand. Peak inward current in the presence of IgG+ATP after 5 minutes IgG incubation was expressed as a fraction of the 4<sup>th</sup> control ATP response. Data were subsequently normalised to a time and concentration matched isotype control antibody response using the equation  $I_{\text{norm}} = I_{\text{IgG}} * (1/I_{\text{isotype}})$  where  $I_{\text{IgG}}$  = fraction of control current for the test IgG and  $I_{\text{isotype}}$  = fraction of control current for the isotype control IgG. Six IgGs were found to significantly inhibit human P2X4 currents; Antibody Nos. 5, 8, 11, 18, 29, and 33 (Figures 3, 4, 8A). Inhibition of P2X4 currents was rapid, occurring at the first time point following IgG addition, whereas the isotype control IgG NIP 228 had no significant effect. IgGs were subsequently tested for function against mouse and cynomolgus P2X4 (Figures 3, 4) and data reported as a mean of n = 3-4 experiments.

Sequences for phage display antibodies are provided in Figure 2. Results of cross reactivity for phage display antibodies between human, cynomolgus monkey, and mouse are provided in Figure 3. Figure 9 provides a structural analysis of the epitope/paratope interface.

Figure 10 provides the sequence of the predicted P2X4 epitope.

#### ***Methods for hybridoma derived mAbs.- Figures 5, 7 & 8***

HEK 293F cells stably expressing either mouse P2X4 (Uniprot # Q9JJX6) or human P2X4 (Uniprot # Q99571) were harvested at 50% confluency using accutase. Cells were then resuspended in 10 ml Freestyle 293F media supplemented with HEPES (10 mM) + apyrase (1U/ml, ATPase/ADPase activity = 1) at a density of  $2-3 \times 10^6$  cells/ml. P2X4 function was assayed using the automated electrophysiology platform QPatch 16X (Sophion) in population patch configuration. Composition of QPatch extracellular buffer (QEB) was (in mM) NaCl (140), KCl (2), MgCl<sub>2</sub> (1) CaCl<sub>2</sub> (2), HEPES (10). Final composition of compound plate extracellular buffer (CPEB2) was NaCl (115.5), KCl (1.3), MgCl<sub>2</sub> (0.66), CaCl<sub>2</sub> (1.32), HEPES (56.1). pH of extracellular buffers was adjusted to 7.4 with NaOH (1 M) and the solutions were 0.2  $\mu$ m filtered. The QPatch intracellular buffer contained (in mM) CsF (140), NaCl (10), EGTA (1), HEPES (10). pH of the intracellular buffer was adjusted to 7.3 with CsOH (1 M) and the solution was 0.2  $\mu$ m filtered. IgGs were titrated to pH 7.4 with NaOH (1 M). After obtaining whole cell configuration, cells were voltage clamped at -50 mV with 70% series resistance compensation employed. The ligand agonist adenosine 5'-triphosphate disodium salt (ATP) (6  $\mu$ M for mouse P2X4, 3  $\mu$ M for human P2X4) in QEB was applied for 3 seconds then washed off with QEB +

aprase (1U/ml). CPEB2 + IgG was then incubated for 3 minutes followed by a second ATP addition. Data were leak subtracted by subtracting the current in the absence of ligand and the magnitude of the P2X4 response measured as the peak inward current in the presence of ligand. The ATP response after IgG addition was expressed as a fraction of the ATP response prior to IgG addition. The hIgG1 NIP 228 TM was used as a control antibody to determine the cutoff for defining functional antibodies. IgGs were initially screened in duplicate (Figure 5, First screen and Figure 7) at mP2X4 and expressed as mean of n = 1-2 experiments. The control antibody NIP 228 TM had a fraction of control current of  $1.08 \pm 0.27$  (Mean  $\pm$  S.D), n = 49. From these data the cutoff for defining functional inhibitory antibodies was set at  $<0.5$  ( $>\sim 2$  standard deviations from the mean). Functional antibodies from the first screen were repeated with a larger sample set (n = 3-4) and data reported as mean  $\pm$  SD (Figure 5).

Results of cross reactivity for hybridoma antibodies between human and mouse are provided at Figures 5 and 7. Sequences for hybridoma antibodies are provided at Figures 6 and 13.

#### **Example 9: *In vivo* testing of monoclonal antibodies to P2X4 in Seltzer model of neuropathic pain**

50 female C57BL/6 mice were used for the studies. All mice underwent insertion of transponders for identification purposes at least 5 days before the start of the study. Mechanical hyperalgesia was determined using an analgesymeter (Randall & Selitto 1957) (Ugo Basile). An increasing force was applied to the dorsal surface of each hind paw in turn until a withdrawal response was observed. The application of force was halted at this point and the weight in grams recorded. Data was expressed as withdrawal threshold in grams for ipsilateral and contralateral paws. Following the establishment of baseline readings mice were divided into 2 groups with approximately equal ipsilateral/contralateral ratios which underwent surgery to partially ligate the sciatic nerve or served as sham operated controls. Operated mice were anaesthetised with isoflurane. Following this approximately 1cm of the left sciatic nerve was exposed by blunt dissection through an incision at the level of the mid thigh. A suture (9/0 Virgin Silk; Ethicon) was then passed through the dorsal third of the nerve and tied tightly. The incision was then closed using glue and the mice were allowed to recover for at least six days prior to

commencement of testing. Sham operated mice underwent the same protocol but following exposure of the nerve the mice were sutured and allowed to recover.

Mice were tested for onset of hyperalgesia on days 7 and 10 post surgery. Any mice showing an ipsilateral/contralateral ratio of greater than 80% were classed as non-responders and removed from the study. Following testing on day 10 mice were further sub-divided into groups giving the final treatment groups;

- A. Group 1: Sham operated + NIP 228 TM 5µg per mouse intra-theal (N=10)
- B. Group 2: Nerve ligated + NIP 228 TM 5µg per mouse intra-theal (N=10)
- C. Group 3: Nerve ligated + Antibody No. 208 5µg per mouse intra-theal (N=10)
- D. Group 4: Nerve ligated + Antibody No. 38 5µg per mouse intra-theal (N=10)

Mice were administered NIP 228 TM (Isotype control) or test molecules on day 13 and were re-tested for changes in mechanical hyperalgesia at 4hrs post dose and also on 1, 2, 4 and 7 days post dose. For dosing mice were anaesthetised with isoflurane. Intra-theal administration was carried out manually into the L4-L6 area of the spinal cord. NIP 228 TM and all test compounds were supplied as 1.02mg/ml = solutions = 1µg per µl = 5µg per mouse.

Ipsilateral and contralateral readings were taken for each animal at each test time and were entered into EXCEL for calculation of ipsilateral/contralateral ratios. Summary data was transferred into PRISM for graphical and statistical analysis. Results were analysed using 2-way ANOVA. Pairwise comparisons where appropriate were made using Tukey's test.

Analysis of the results showed that partial ligation of the sciatic nerve caused a mechanical hyperalgesia which manifested as a significant reduction in the ipsilateral/contralateral ratio on day 7 and 10 when compared to sham operated controls. Following treatment with NIP228, operated mice did not show any change in the level of mechanical hyperalgesia from pre-dose levels indicating a lack of effect of the isotype control on mechanical hyperalgesia. The administration of Antibody No. 208 produced a significant reversal which was significant for up to 4 days post dose after which the response returned to baseline levels. Similar effects were seen with Antibody No. 38 (Fig13).

**Example 10: Generation of mouse anti-human P2X4 antibodies by hybridoma technology**

**Methods for mouse anti-human P2X4 antibody generation** were carried out in the same way as described in the previous section of rat anti-murine P2X4 antibody generation, other than the following differences:

***Immunisations***

Human P2X4 (hP2X4) transfected HEK 293F and XS63 cells were used to immunise CD1 mice in three groups. In group 1, mice were immunised with hP2X4 transfected HEK 293F cells, group 2 mice were immunised with hP2X4 transfected XS63 cells, and group 3 mice were immunised by alternating hP2X4 transfected XS63 cells and hP2X4 transfected HEK 293F cells.

hP2X4 transfected cells were re-suspended at  $1 \times 10^8$ /mL and emulsified with equal volumes of complete Freund's adjuvant, and injected into mice at two sites, 100  $\mu$ L per site. For the subsequent 3 injections, the same number of cells was emulsified in Freund's incomplete adjuvant and injections were performed as above. The last boost was carried out on day 24, injecting 200  $\mu$ L of transfected cells at  $1 \times 10^8$ /mL intraperitoneally.

***Assessment of mouse immune response to hP2X4 using a cell-based DELFIA***

The serum IgG titres to hP2X4 were determined by a cell-based time-resolved fluorescence assays (DELFI) using parental HEK 293F cells and hP2X4 transfected HEK 293F cells.

***Monoclonal mouse IgG isolation***

Lymphoid cells isolated from spleens and lymph nodes were fused with SP2/0 myeloma cells using an electrofusion method. The fusions were plated out into semi-solid selection media containing FITC conjugated goat anti-mouse IgG.

***Cell binding assay for mouse IgGs***

Supernatants were initially screened for IgGs that specifically bound to hP2X4 using both the hP2X4 expressing HEK 293F and XS63 cells, and parental HEK 293F cells. The IgGs that showed specific binding to hP2X4, and no binding to parental HEK293F cells, were selected for further specificity testing on mouse P2X4 (mP2X4) HEK 293F cells. IgGs which specifically  
5 bound to hP2X4 or to both hP2X4 and mP2X4 were selected for antibody purification and functional analysis by electrophysiology.

#### ***DNA sequencing and purification of mouse IgGs***

10 Messenger RNA (mRNA) was extracted from hybridoma cells using magnetic oligo (dT) particles and reverse transcribed into cDNA. Polymerase chain reaction (PCR) amplification was performed using poly-C and constant region VH or VL primers specific to all mouse IgG subclasses.

Mouse IgGs of all subclasses (IgG1, IgG2a, IgG2b and IgG3) were purified from overgrown cell  
15 culture supernatants on ProPlus resin (Phynexus).

#### ***Functional screening by electrophysiology***

HEK 293F cells stably expressing human P2X4 (Uniprot # Q99571) were harvested at 50%  
20 confluency using accutase. Cells were then resuspended in 10 ml Freestyle 293F media supplemented with HEPES (10 mM) + apyrase (1U/ml, ATPase/ADPase activity = 1) at a density of  $2-3 \times 10^6$  cells/ml. P2X4 function was assayed using the automated electrophysiology platform QPatch 16X (Sophion) in population patch configuration. Composition of QPatch extracellular buffer (QEB) was (in mM) NaCl (140), KCl (2), MgCl<sub>2</sub> (1) CaCl<sub>2</sub> (2), HEPES (10).  
25 Final composition of compound plate extracellular buffer (CPEB2) was NaCl (115.5), KCl (1.3), MgCl<sub>2</sub> (0.66), CaCl<sub>2</sub> (1.32), HEPES (56.1). pH of extracellular buffers was adjusted to 7.4 with NaOH (1 M) and the solutions were 0.2 µm filtered. The QPatch intracellular buffer contained (in mM) CsF (140), NaCl (10), EGTA (1), HEPES (10). pH of the intracellular buffer was adjusted to 7.3 with CsOH (1 M) and the solution was 0.2 µm filtered. IgGs were titrated to pH  
30 7.4 with NaOH (1 M). After obtaining whole cell configuration, cells were voltage clamped at -50 mV with 70% series resistance compensation employed. The ligand agonist adenosine 5'-triphosphate disodium salt (ATP, 3 µM) in QEB was applied for 3 seconds then washed off with

QEB + apyrase (1U/ml). CPEB2 + IgG was then incubated for 3 minutes followed by a second ATP addition. Data were leak subtracted by subtracting the current in the absence of ligand and the magnitude of the P2X4 response measured as the peak inward current in the presence of ligand. The ATP response after IgG addition was expressed as a fraction of the ATP response prior to IgG addition. The hIgG1 NIP 228 TM was used as a control antibody to determine the cutoff for defining functional antibodies. Results are provided at Figure 23. Antibody sequences are provided in Figure 13.

### 10 Example 11: Affinity maturation of Antibody 11

Antibody No. 11 was optimised for affinity via two approaches either; targeted or random mutagenesis followed by affinity-based phage display selections. In the targeted approach, large scFv-phage libraries derived from the lead clone were created by oligonucleotide-directed mutagenesis of the variable heavy (VH) complementarity determining regions 3 (CDR3) and light (VL) chain CDR3 using standard molecular biology techniques as described (*Clackson, T. and Lowman, H.B. Phage Display – A Practical Approach, 2004. Oxford University Press*). The libraries were subjected to affinity-based phage display selections in order to select variants with higher affinity for human P2X4. The selections were performed essentially as described previously in Example 3 with the exception of lowering the concentration of immobilised human P2X4 over four rounds of selection (10µg/ml-1.25µg/ml). Antibodies with improved affinity were identified in a competition assay based on Antibody 11 binding to huP2X4 expressing cells (described in Example 12). To generate further affinity improvement, CDR mutations from improved antibodies were recombined into new scFvs using standard molecular biology techniques.

Antibody 11 was also optimised using a random mutagenesis approach to identify key residues within the entire variable domain that may improve binding to human P2X4. Such a technique is described by Gram *et al.* [Gram *et al.*, 1992, *Proc. Natl. Acad. Sci., USA*, 89:3576-3580], who used error-prone PCR. In some embodiments one or two amino acid substitutions are made within an entire variable domain or set of CDRs. The generated library was subjected to affinity-based selections as described for the targeted selections outlined above.

Exemplary antibodies from this selection method are disclosed herein as Antibodies 287 to 315, and an alignment of their sequences is shown in Figure 12.

## 5 **Example 12: Identification of higher affinity antibodies against human P2X4**

Phage display selection outputs described in example 11, were screened for activity in a competition assay based on Antibody 11 binding to huP2X4 expressing cells. Briefly Antibody 11 IgG was labelled with DyLight® 650 using a Lightning-Link® Rapid DyLight® 650 conjugation kit following the manufacturer's instructions (Innova Biosciences Ltd). Bacterially expressed scFv were collected into 0.2M HEPES buffer pH7.4, 0.5 mM EDTA and 0.5 M sucrose as peri plasmic extracts and added to the assay plate (Corning® 3655) together with assay buffer (HBSS, 0.1% BSA, 1U/ml apyrase, either with or without 20mM HEPES). Antibody 11-DyLight® 650 was added to each well except the wells used to define the background binding, to a final concentration of 2nM. HEK293F huP2X4 cells were added to each well at a final density of approximately 2000 cells per well. Plates were covered and incubated at room temperature for 2 to 3 hours before reading on a mirrorball® plate reader (TTP Labtech, Ltd) and determining the total FL3 fluorescence per well (Median (mean intensity) fluorescence multiplied by the number of objects). Individual events were gated on size and fluorescence and a minimum object number of greater than 25 was used to determine wells with sufficient events to report a FL3 total value. % specific binding was calculated for each well using the following equation, maximal FL3 total values were defined from wells that did not receive any scFv but did receive peri plasmic sample buffer:

$$25 \quad \% \text{ specific binding} = \frac{\text{sample FL3 total} - \text{background FL3 total}}{\text{maximal FL3 total} - \text{background FL3 total}} \times 100$$

Samples where the binding signal was lower than 85% specific binding were selected for sequencing and sequence unique hits were generated as purified scFv.

To confirm the inhibition of these scFv antibodies, purified scFv antibodies were diluted in assay buffer described above to generate a dilution series and the diluted samples were added to the assay plate before the addition of Antibody 11- DyLight® 650 to a final concentration of 2nM, followed by approximately 2000 HEK293F huP2X4 cells per well. Plates were incubated at

room temperature for 2 to 3 hours before being read on the mirrorball® plate reader. Data was analysed as described above and scFv clones showing inhibition were generated as full IgG antibodies.

5

**Example 13: Identification of antibodies with improved potency against human P2X4 using the human P2X4 1321N1 cell line FLIPR® assay**

Antibodies identified in the Antibody 11 competition assay described in example 12 were generated as purified IgG and titrated to generate a dilution series. These antibodies were diluted in assay buffer containing HBSS and 0.1% BSA and pre-incubated with 1321N1 cells expressing huP2X4 for 30mins where the cells had previously been loaded with Fluo-4 NW calcium dye (Molecular Probes™, Life Technologies) following the manufacturer's instructions. P2X4 was activated by the addition of 1µM ATP diluted in assay buffer and the resulting rise in intracellular calcium was detected by the calcium dye and measured by an increase in fluorescence using the FLIPR® Tetra plate reader (Molecular Devices, LLC). Data was calculated to determine the maximum fluorescence observed over the background fluorescence for the duration of the assay. These data were then analysed to determine % maximal response over the buffer response alone seen in wells where ATP was omitted, using the following equation:

$$\% \text{ maximal response} = \frac{\text{sample response} - \text{buffer response}}{\text{total response} - \text{buffer response}} \times 100$$

Data was analysed in Prism (GraphPad Software, Inc) to determine IC<sub>50</sub> values using the following equation:

$$Y = \text{Bottom} + (\text{Top} - \text{Bottom}) / (1 + 10^{((\text{LogIC}_{50} - X) * \text{HillSlope}))}$$

To enable ranking of antibodies the top and bottom of the curves were constrained to 100 and 0 respectively. Geometric means of the IC<sub>50</sub> values for the antibodies tested are listed in Figure 15 and an example of the IC<sub>50</sub> curves for two antibodies are shown in Figure 19 together with an isotype control antibody

**Example 14:** Identification of antibodies with improved potency against human P2X4 using the HEK 293F huP2X4 cell line on the automated electrophysiology platform Qpatch 16X.

HEK 293F cells stably expressing human P2X4, were harvested at 50% confluency using  
 5 accutase. Cells were then resuspended in 10 ml Freestyle 293F media supplemented with HEPES  
 (10 mM) + apyrase (1U/ml, ATPase/ADPase activity = 1) at a density of  $2-3 \times 10^6$  cells/ml. P2X4  
 function was assayed using the automated electrophysiology platform QPatch 16X (Sophion) in  
 population patch configuration. Composition of QPatch extracellular buffer (QEB) was (in mM)  
 NaCl (140), KCl (2),  $MgCl_2$  (1)  $CaCl_2$  (2), HEPES (10). pH of extracellular buffers was adjusted  
 10 to 7.4 with NaOH (1 M), osmolarity was adjusted to 300 mOsm with sucrose and the solutions  
 were  $0.2 \mu m$  filtered. The QPatch intracellular buffer (QIB) contained (in mM) CsF (140), NaCl  
 (10), EGTA (1), HEPES (10). pH of the intracellular buffer was adjusted to 7.3 with CsOH (1  
 M) and the solution was  $0.2 \mu m$  filtered. IgGs were titrated to pH 7.4 with NaOH (1 M).

For determination of the potency of optimized variants of Antibody 11, IgGs were  
 15 serially diluted in QEB + 0.1% bovine serum albumin and tested for function on Qpatch 16X in  
 population patch configuration. Extracellular buffer was QEB, intracellular buffer was QIB and  
 ATP wash buffer was QEB + apyrase (1U/ml). In this assay, ATP ( $3 \mu M$ ) was applied every 10  
 mins for 3 s with a total of 5 applications per experiment. The first two ATP additions (ATP 1 &  
 ATP 2) were preceded by preincubation for 5 mins with QEB buffer + 0.1 % BSA whereas the  
 20 following three ATP additions were preceded by 5 mins incubation with ascending doses of IgG.  
 Log and half log doses of IgG were interleaved in post analysis to generate 6 point dose response  
 curves (dose range 100 – 0.3 nM). Data were leak subtracted by subtracting the current in the  
 absence of ligand and the magnitude of the P2X4 response measured as the peak inward current  
 in the presence of ligand. The peak inward current in response to ATP was expressed as fraction  
 25 of control current (ATP2) and labeled as  $I/I_{basal}$ . Data were fit in Prism using a log (inhibitor) vs.  
 response - Variable slope (four parameters) equation.  $Y = Bottom + (Top - Bottom) / (1 + 10^{((LogIC50 - X) * HillSlope)})$ . The top of the IgG dose response curves was defined  
 by the response to 0.3 nM NIP 228 and constrained to this value. The bottom of the curve was  
 constrained such that it was greater than zero. See Figure 14-15.

30

**Example 15** Potency determination of hybridoma derived antibodies at mouse and human P2X4. HEK 293F cells expressing P2X4 were handled as in example 8. Potency of hybridoma derived IgGs was assayed on Qpatch 16X in population patch configuration. For determination of IgG potency, IgGs were serially diluted in PBS + 0.1% bovine serum albumin and tested for function on Qpatch 16X in population patch configuration. IgGs were then diluted 1:3 in QEB + 0.1% BSA resulting in a final buffer composition of NaCl (137.6), KCl (2.2), MgCl<sub>2</sub> (0.66), CaCl<sub>2</sub> (1.3), HEPES (6.6), KH<sub>2</sub>PO<sub>4</sub> (0.49), NaH<sub>2</sub>PO<sub>4</sub> (2.66), BSA (0.1%) equivalent to CPEB1. Extracellular buffer was QEB, intracellular buffer was QIB and ATP wash buffer was QEB + apyrase (1U/ml). In this assay, ATP (3 µM) was applied every 10 mins for 3 s with a total of 5 applications per experiment. The first two ATP additions (ATP 1 & ATP 2) were preceded by preincubation for 5 mins with CPEB1 + 0.1 % BSA whereas the following three ATP additions were preceded by 5 mins incubation with ascending doses of IgG. Log and half log doses were interleaved in post analysis to generate 6 point dose response curves. Data were leak subtracted by subtracting the current in the absence of ligand and the magnitude of the P2X4 response measured as the peak inward current in the presence of ligand. The peak inward current in response to ATP was expressed as fraction of control current (ATP2). Data were fit in Prism using a log (inhibitor) vs. response - Variable slope (four parameters) equation.  $Y = \text{Bottom} + (\text{Top} - \text{Bottom}) / (1 + 10^{((\text{LogIC}_{50} - X) * \text{HillSlope}))}$ . The top of the IgG dose response curves was constrained to 1 whereas the bottom of the curve was constrained such that it was greater than zero. See Figure 16.

**Example 16** Efficacy of mouse reactive antibodies at native mouse microglial P2X4

Culture of mouse microglia:

Primary mouse microglia were cultured from C57 neonatal pups, P2. Brains were removed from the skulls of mice and kept in media (DMEM + 10% FCS + pen/strep). They were then rolled across filter paper to remove the sticky vasculature and meninges before placing in 20 ml fresh media and triturating to give a single cell suspension. Cells were then filter sterilised through a 40 µm cell strainer then centrifuged at 1200rpm for 5 min. Cells were then resuspended in 40ml media per flask at 4 brains per T175 flask and cultured for 1 week. After this, the media was supplemented with GM-CSF (5 ng/ml) and the cells cultured for a further week. Microglia were removed by shaking overnight in an orbital shaker incubator (no CO<sub>2</sub>) with HEPES supplemented in the media (20 mM). Purified microglia were centrifuged at 1200 rpm for 5 mins

and resuspended in 20 ml DMEM + 10% FCS + pen/strep growth media. Cells were counted and seeded in ultra low bind T75 cell culture flasks (Corning) at  $7 \times 10^6$  cells/flask. Microglia were then maintained in culture for 1-7 days before being used for Qpatch 16X electrophysiology assays or FLIPR calcium imaging assays.

5

#### Cell handling Qpatch:

1 x T75 flask was washed twice with dPBS and cells were harvested using accutase treatment for 5-10 mins. Cells were then resuspended in 293F Freestyle media + 20 mM HEPES + 1U/ml accutase (10 ml) and spun down at 800 rpm for 5 mins. Cells were then resuspended in 3 ml  
10 293F Freestyle media + 20 mM HEPES + 1U/ml accutase and 1 ml of cell suspension used per experiment.

Qpatch 16X was used in population patch configuration and cells voltage clamped at -70 mV. Cells were perfused with either a control antibody or test antibody for 5 minutes before ATP (30  
15  $\mu$ M) was applied. Current in the absence of ATP was subtracted from all data. Inward current in response to ATP was measured (see Figure 15). External buffer was QEB and internal buffer was QIB. See Figure 17 & 18.

#### FLIPR:

20 Microglia were plated in Cell Coat Poly-D-Lysine coated 384 well plates (black, uclear) with 30  $\mu$ l per well and cultured in a humidified incubator at 37 °C for 48 hours.

Media was removed and replaced with 20  $\mu$ l per well of HBSS buffer + 20 mM HEPES + 0.1% BSA, supplemented with Screen Quest™ Fluo-8 No Wash Calcium Assay Kit (AAT Bioquest, Inc.) as per the manufacturers instructions. Cells were then incubated at 37°C for 30 mins then  
25 returned to room temperature for 15 mins before assaying on FLIPR (Molecular devices). Ivermectin (12  $\mu$ M) was made up in a further 384 well compound plate (Compound plate 1). IgGs were made up in PBS + 0.1 % BSA (compound plate 2). ATP (30  $\mu$ M) was made up in HBSS + 20 mM HEPES + 0.1 % BSA in a separate 384 well compound plate (Compound plate 3 ). Fluo-8 was excited at a wavelength of 470-495 nm and the emitted light measured at a  
30 wavelength of 515-575 nm. Camera gain was adjusted to give 1000 counts at rest with an exposure of 0.4 s. 10  $\mu$ l of solution from compound plate 1 was added to the cells and the

fluorescence measured. After 5 mins incubation, 10 ul of solution from compound plate 2 was added. 15 min later, ATP (5 uM final) was added and the peak end fluorescence measured between 200-300 sec post ATP addition. Fluorescence counts were normalised to the ATP response in the absence of antibody (minus background fluorescence) and plotted as % of ATP response (See figure 21). 10 point dose response curves for each IgG were constructed from duplicate wells and the data fit in Prism using a log (inhibitor) vs. response - Variable slope (four parameters) equation.  $Y = \text{Bottom} + (\text{Top} - \text{Bottom}) / (1 + 10^{((\text{LogIC50} - X) * \text{HillSlope}))}$ . See Figure 20.

#### 10 Example 17: Functional effect of P2X4 antibodies on human monocyte derived macrophages.

##### Cell culture

Human monocytes were isolated from the mononuclear fraction of peripheral blood by centrifugation on a Ficoll-Paque gradient. Cells were then purified by incubating in a T175 cell culture flask in cell culture media in the absence of serum for 1 hour. Non-adherent cells were removed and the remaining cells grown in RPMI Glutamax I media supplemented with 10% FCS (HI/GI) + 1% P/S + 100 ng/ml M-CSF for 7 days. Cells were fed on day 2-3 by adding an additional 10 ml of media. Macrophage were harvested by accutase treatment for 10 mins followed by cell scraping and replated in ultra-low bind T75 flasks at 6e6 cells per flask. Cells were then cultured for a further 1-10 days before being used for electrophysiological recording. On the day of experiment, cells were harvested with accutase and resuspended in 3 ml CHO ACF media + 20 mM HEPES. 1ml of cell suspension was used per experiment on Qpatch 16X in population patch configuration. Qpatch 16X assay parameters were as described for example 16. Nippon antagonist refers to 1H-naphtho[1,2-b][1,4]diazepine-2,4(3H,5H)-dione (described in Patents WO-2010/093061 and EP2397480A1 See Figures 21 & 22.

##### Other Embodiments

From the foregoing description, it will be apparent that variations and modifications may be made to the invention described herein to adopt it to various usages and conditions. Such embodiments are also within the scope of the following claims.

The recitation of a listing of elements in any definition of a variable herein includes definitions of that variable as any single element or combination (or subcombination) of listed elements. The recitation of an embodiment herein includes that embodiment as any single embodiment or in combination with any other embodiments or portions thereof.

5 All patents and publications mentioned in this specification are herein incorporated by reference to the same extent as if each independent patent and publication was specifically and individually indicated to be incorporated by reference.

0 Throughout the description and claims of the specification, the word “comprise” and variations of the word, such as “comprising” and “comprises”, is not intended to exclude other additives, components, integers or steps.

A reference herein to a patent document or other matter which is given as prior art is not to be taken as admission that the document or matter was known or that the information it contains was part of the common general knowledge as at the priority date of any of the claims.

What is claimed is:

1. An antibody or antigen binding fragment thereof that specifically binds a human P2X4 polypeptide and modulates channel activity, wherein the antibody or antigen binding fragment thereof is a P2X4 antagonist and binds an epitope comprising human P2X4 amino acids 110-166.
2. The antibody or antigen binding fragment of claim 1, wherein the antibody reduces P2X4 biological activity by at least about 10, 25, 50, 75, 85, 90 or 95%.
3. The antibody or antigen binding fragment of claim 1 or claim 2, wherein the antibody binds an epitope comprising one or more human P2X4 amino acids selected from the group consisting of amino acids 118, 122-139, 145, 159, 180, 183, 184, 231, and 244.
4. The antibody or antigen binding fragment of any one of claims 1 to 3, wherein an amino acid substitution at position 131 of P2X4 reduces or eliminates antibody binding to a human P2X4 polypeptide.
5. The antibody or antigen binding fragment of claim 4, wherein the serine at position 131 of human P2X4 is substituted by Asparagine.
6. The antibody or antigen binding fragment of any one of claims 1 to 5, wherein the antibody or fragment thereof comprises a VH comprising:
  - a. a heavy chain variable region CDR1 comprising the sequence: SX<sub>1</sub>AMS where X<sub>1</sub> is Y or F;
  - b. a heavy chain variable region CDR2 comprising the sequence: AISGSG X<sub>1</sub>STYYADSVKG where X<sub>1</sub> is S or G;
  - c. a heavy chain variable region CDR3 comprising the sequence: X<sub>1</sub>X<sub>2</sub>DX<sub>3</sub>WSX<sub>4</sub>X<sub>5</sub>X<sub>6</sub>X<sub>7</sub>X<sub>8</sub>TAFDL, where X<sub>1</sub> is H, D or Q; X<sub>2</sub> is W, M, F, H, or R; X<sub>3</sub> is W, Y or F; X<sub>4</sub> is T, N, G, or P; X<sub>5</sub> is R, A, S, G, or Y; X<sub>6</sub> is S, P, N or T; X<sub>7</sub> is G, S, R, or K; X<sub>8</sub> is P, M, A or L.
optionally in combination with a VL comprising
  - a. a light chain variable region CDR1 comprising the sequence SGDALPRQYAY
  - b. a light chain variable region CDR2 comprising the sequence KDSX<sub>1</sub>RPS where X<sub>1</sub> is E or F.

c. a light chain variable region CDR3 comprising the sequence QSADSSGTYX<sub>1</sub>V.  
Where X<sub>1</sub> is V or A.

7. The antibody or antigen binding fragment of claim 6, wherein the antibody or fragment thereof comprises a VH comprising:

- a. a heavy chain variable region CDR1 comprising the sequence: SFAMS;
- b. a heavy chain variable region CDR2 comprising the sequence: AISGSG GSTYYADSVKG;
- c. a heavy chain variable region CDR3 comprising the sequence: QFDYWSTYSGPTAFDL;  
in combination with a VL comprising
  - a. a light chain variable region CDR1 comprising the sequence SGDALPRQYAY
  - b. a light chain variable region CDR2 comprising the sequence KDSERPS
  - c. a light chain variable region CDR3 comprising the sequence QSADSSGTYVV.

8. The antibody or antigen binding fragment of any one of claims 1 to 7, wherein the antibody or antigen binding fragment does not bind to a mutant form of human P2X4 having an amino acid substitution at position 131.

9. The antibody or antigen binding fragment of claim 8, wherein the mutant form comprises an Asparagine at position 131.

10. The antibody or antigen binding fragment one of any of claims 1 to 9, wherein the antigen binding fragment thereof is a single chain antibody, a single chain variable fragment (scFv), a Fab fragment, or a F(ab')<sub>2</sub> fragment.

11. A polynucleotide encoding the antibody or antigen binding fragment thereof of any one of claims 1 to 10.

12. A vector comprising the polynucleotide of claim 11.

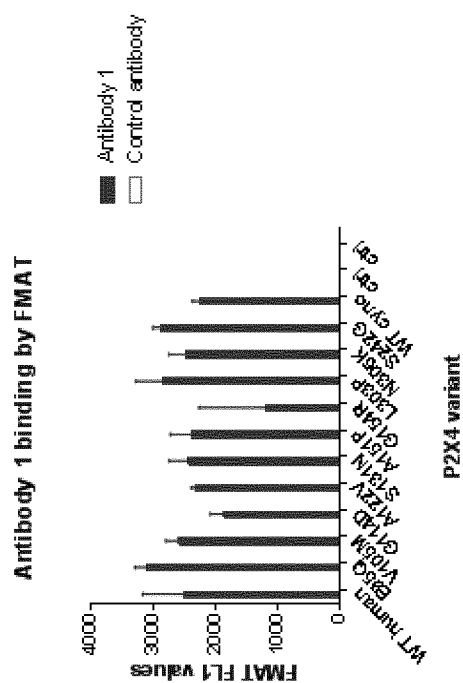
13. A host cell comprising the vector of claim 12.

14. A method for treating neuropathic pain, the method comprising administering to a patient in need thereof an effective amount of an antibody or antigen binding fragment thereof that specifically binds P2X4 and modulates its ion channel function, wherein the antibody or antigen binding fragment is as defined in any one of claims 1 to 10.

15. The method of claim 14, wherein the antibody or antigen binding fragment thereof is administered by intrathecal delivery.

16. Use of an antibody of any one of claims 1 to 10 or antigen binding fragment thereof in the manufacture of a medicament for treating neuropathic pain.

Figure 1A



## Figure 1B

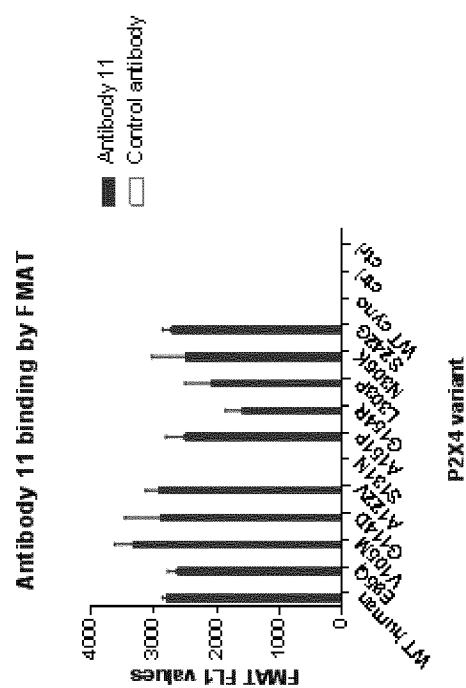
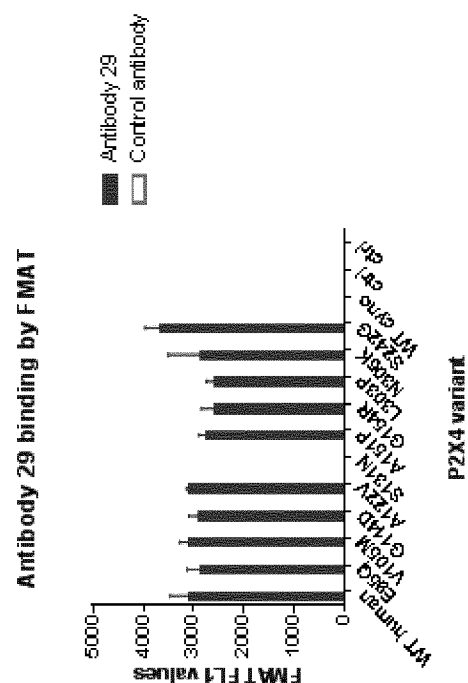
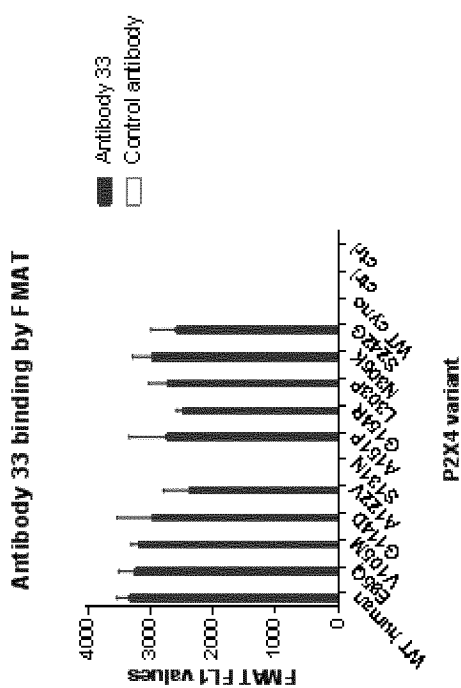


Figure 1C



## Figure 1D



### **Figure 2 – part 1: Phage display P2X4 Binding – Antibodies (Abs) VH sequences**

| Antibody number | FW 1 |   |   |   |   |   |   |   |   |    | CDR 1 |    |    |    |    |    |    |    |    |    | FW 2 |    |    |    |    |    |    |    |    |    | CDR 2 |    |    |    |    |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |
|-----------------|------|---|---|---|---|---|---|---|---|----|-------|----|----|----|----|----|----|----|----|----|------|----|----|----|----|----|----|----|----|----|-------|----|----|----|----|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|
|                 | 1    | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11    | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21   | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31    | 32 | 33 | 34 | 35 | a | b | c | d | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | a | b | c | d | e | f | 53 | 54 | 55 | 56 | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 |
| 1               | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | G  | S  | L  | R  | L  | S  | C  | A    | A  | S  | G  | F  | T  | F  | S  | G  | Y  | A     | M  | S  | -  | -  | - | W | V | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | - | S | G | S | T | Y | Y  | A  | D  | S  | V  | K  | G  |    |    |    |    |    |
| 2               | E    | V | Q | L | V | E | I | G | G | L  | V     | K  | P  | G  | S  | L  | R  | L  | S  | C  | A    | A  | S  | G  | F  | T  | F  | S  | N  | A  | W     | M  | S  | -  | -  | - | W | V | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | V  | G  | R  | I  | K  | S  | K  | I  | - | - | - | D | G | T | I  | D  | Y  | A  | A  | P  | V  | K  | G  |    |    |    |
| 3               | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | G  | S  | L  | R  | L  | S  | C  | A    | A  | S  | G  | F  | T  | F  | S  | S  | Y  | A     | M  | S  | -  | -  | - | W | V | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | - | S | G | S | T | Y | Y  | A  | D  | S  | V  | K  | G  |    |    |    |    |    |
| 4               | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | G  | S  | L  | R  | L  | S  | C  | A    | A  | S  | G  | F  | T  | F  | S  | S  | Y  | A     | M  | S  | -  | -  | - | W | V | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | - | S | G | S | T | Y | Y  | A  | D  | S  | V  | K  | G  |    |    |    |    |    |
| 5               | Q    | V | L | V | Q | S | G | A | E | V  | K     | K  | P  | G  | E  | S  | L  | R  | I  | S  | C    | K  | G  | S  | G  | Y  | S  | F  | T  | S  | Y     | W  | I  | G  | -  | - | - | W | V | R  | Q  | M  | P  | G  | K  | G  | L  | E  | W  | M  | G  | I  | I  | Y  | P  | -  | - | - | G | D | S | T | R  | Y  | S  | P  | S  | F  | Q  | G  |    |    |    |    |
| 6               | E    | V | Q | L | V | S | G | A | E | L  | K     | K  | P  | S  | E  | T  | S  | L  | R  | I  | S    | C  | Q  | G  | S  | G  | Y  | S  | F  | T  | S     | H  | M  | I  | T  | - | - | - | W | V  | R  | Q  | P  | S  | G  | K  | G  | L  | E  | W  | M  | G  | I  | I  | D  | P  | - | - | - | S | D | S | Y  | T  | N  | Q  | N  | P  | S  | F  | Q  | G  |    |    |
| 7               | Q    | V | Q | L | Q | W | G | A | G | L  | L     | K  | P  | S  | E  | T  | S  | L  | T  | C  | G    | V  | R  | G  | S  | L  | S  | D  | F  | Y  | W     | I  | T  | -  | -  | - | W | I | R | Q  | S  | P  | R  | G  | G  | L  | E  | W  | I  | G  | E  | I  | N  | -  | -  | -  | H | S | G | D | I | N | Y  | N  | P  | S  | L  | K  | S  |    |    |    |    |    |
| 8               | E    | V | Q | L | V | S | G | G | L | V  | Q     | P  | G  | R  | S  | L  | R  | L  | S  | C  | T    | A  | S  | G  | F  | T  | F  | D  | Y  | S  | M     | H  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | I  | S  | W  | -  | -  | -  | S  | G | S | I | G | Y | A | D  | S  | V  | K  | G  |    |    |    |    |    |    |    |
| 9               | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 10              | Q    | V | L | E | S | G | G | V | V | P  | G     | R  | S  | L  | R  | L  | S  | C  | A  | A  | S    | G  | F  | T  | F  | S  | S  | Y  | G  | M  | H     | -  | -  | -  | W  | V | R | Q | A | P  | G  | K  | G  | L  | E  | W  | V  | A  | V  | I  | W  | Y  | -  | -  | -  | D  | G | S | N | K | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 11              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 12              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 13              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | E  | G  |    |    |    |    |    |    |
| 14              | E    | V | Q | L | V | S | G | G | V | V  | Q     | P  | G  | R  | S  | L  | R  | L  | S  | C  | A    | A  | S  | G  | F  | T  | F  | S  | S  | Y  | A     | M  | H  | -  | -  | - | W | V | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | V  | A  | V  | I  | S  | Y  | -  | -  | - | D | G | S | N | K | Y  | Y  | A  | D  | S  | V  | K  | G  |    |    |    |    |
| 15              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 16              | E    | V | Q | L | V | S | G | G | L | V  | Q     | P  | G  | R  | S  | L  | R  | L  | S  | C  | T    | A  | S  | G  | F  | T  | F  | S  | D  | Y  | S     | M  | H  | -  | -  | - | W | V | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | I  | S  | W  | -  | -  | -  | S | S | G | S | I | G | Y  | A  | D  | S  | V  | K  | G  |    |    |    |    |    |
| 17              | Q    | V | L | V | Q | S | G | A | E | V  | R     | K  | P  | G  | A  | S  | V  | K  | V  | S  | C    | K  | A  | S  | G  | Y  | F  | T  | G  | F  | F     | L  | H  | -  | -  | - | W | V | R | Q  | A  | P  | Q  | G  | L  | E  | W  | M  | G  | W  | I  | N  | P  | -  | -  | -  | N | S | G | A | I | Q | Y  | A  | R  | K  | F  | E  | A  |    |    |    |    |    |
| 18              | E    | V | Q | L | V | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | R  | Y  | W  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | A  | N  | I  | K  | E  | -  | -  | -  | D | G | S | E | K | N | V  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 19              | Q    | V | L | Q | S | G | A | E | V | R  | K     | P  | G  | S  | V  | K  | V  | S  | C  | K  | A    | S  | G  | G  | T  | F  | S  | S  | Y  | G  | I     | S  | -  | -  | -  | W | V | R | Q | V  | P  | G  | Q  | G  | L  | E  | W  | M  | G  | I  | I  | P  | -  | -  | -  | R  | F | G | T | A | N | N | V  | D  | S  | V  | K  | Q  | D  |    |    |    |    |    |
| 20              | Q    | V | L | V | S | G | A | E | V | K  | T     | P  | G  | A  | S  | V  | K  | V  | S  | C  | K    | A  | S  | G  | Y  | S  | F  | T  | R  | Y  | G     | F  | S  | -  | -  | - | W | V | R | Q  | A  | P  | G  | Q  | E  | L  | E  | W  | M  | G  | I  | S  | A  | -  | -  | -  | Y | N | G | N | T | N | Y  | A  | Q  | K  | F  | Q  | G  |    |    |    |    |    |
| 21              | Q    | V | Q | L | Q | S | G | T | E | V  | K     | K  | P  | G  | S  | V  | K  | V  | S  | C  | K    | A  | S  | G  | Y  | T  | F  | T  | S  | F  | E     | V  | H  | -  | -  | - | W | V | R | Q  | A  | P  | Q  | G  | L  | E  | W  | M  | G  | W  | M  | N  | P  | -  | -  | -  | N | S | N | N | T | D | Y  | A  | Q  | K  | F  | Q  | G  |    |    |    |    |    |
| 22              | Q    | V | L | V | Q | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | R  | G  | L  | E  | W  | V  | S  | I  | S  | A  | -  | -  | -  | S  | G | N | T | Y | Y | A | D  | S  | V  | K  | G  |    |    |    |    |    |    |    |
| 23              | Q    | V | L | Q | W | G | P | G | L | V  | K     | P  | S  | E  | T  | S  | L  | T  | C  | G  | V    | R  | G  | S  | L  | S  | D  | F  | Y  | W  | T     | -  | -  | -  | W  | I | R | Q | S | P  | R  | G  | L  | E  | W  | I  | G  | E  | I  | N  | -  | -  | -  | D  | R  | G  | S | T | N | Y | N | P | S  | L  | K  | S  |    |    |    |    |    |    |    |    |
| 24              | E    | V | Q | L | V | S | G | G | V | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | D  | Y  | A  | M     | H  | -  | -  | -  | W | V | R | Q | A  | P  | K  | G  | L  | E  | W  | V  | S  | R  | I  | S  | R  | -  | -  | -  | D  | G | S | M | T | E | Y | A  | D  | S  | A  | K  | G  |    |    |    |    |    |    |
| 25              | E    | V | Q | L | V | E | I | G | G | L  | V     | K  | P  | G  | S  | L  | R  | L  | S  | C  | A    | A  | S  | G  | F  | T  | F  | S  | D  | Y  | D     | M  | S  | -  | -  | - | W | I | R | Q  | A  | P  | G  | K  | G  | L  | E  | W  | L  | S  | I  | S  | N  | -  | -  | -  | S | G | T | F | N | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 26              | Q    | V | L | V | Q | S | G | A | E | V  | K     | K  | P  | G  | S  | V  | K  | V  | S  | C  | K    | A  | S  | G  | G  | T  | F  | S  | N  | S  | P     | I  | N  | -  | -  | - | W | L | R | Q  | A  | P  | Q  | G  | L  | E  | W  | M  | G  | S  | I  | P  | -  | -  | -  | S  | F | G | T | A | N | Y | A  | Q  | R  | F  | Q  | G  |    |    |    |    |    |    |
| 27              | Q    | V | L | V | Q | S | G | A | E | V  | K     | K  | P  | G  | A  | S  | V  | I  | L  | S  | C    | E  | A  | S  | E  | Y  | T  | F  | T  | N  | Y     | I  | H  | -  | -  | - | W | V | R | Q  | A  | P  | S  | Q  | G  | L  | Q  | W  | M  | G  | V  | I  | K  | P  | -  | -  | - | N | D | G | T | K | N  | V  | A  | Q  | K  | F  | Q  | G  |    |    |    |    |
| 28              | Q    | V | L | Q | Q | S | G | A | E | L  | K     | K  | P  | G  | S  | V  | K  | V  | S  | C  | K    | I  | S  | G  | G  | T  | F  | S  | S  | H  | A     | I  | N  | -  | -  | - | W | V | R | Q  | A  | P  | Q  | G  | L  | E  | W  | M  | G  | A  | I  | P  | -  | -  | -  | V  | F | G | T | H | S | A | Q  | K  | F  | E  | D  | G  |    |    |    |    |    |    |
| 29              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 30              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 31              | E    | V | Q | L | V | Q | S | P | E | V  | R     | K  | P  | G  | A  | S  | V  | K  | V  | S  | C    | Q  | A  | S  | G  | Y  | S  | F  | P  | N  | Y     | I  | T  | -  | -  | - | W | V | R | Q  | A  | P  | G  | R  | G  | L  | E  | W  | V  | G  | W  | I  | A  | -  | -  | -  | Y | I | G | D | T | K | Y  | A  | Q  | N  | F  | Q  | D  |    |    |    |    |    |
| 32              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  | G  | K  | G  | L  | E  | W  | V  | S  | A  | I  | S  | G  | -  | -  | -  | S | G | S | T | Y | Y | A  | D  | S  | V  | K  | G  |    |    |    |    |    |    |
| 33              | E    | V | Q | L | E | S | G | G | L | V  | Q     | P  | G  | S  | L  | R  | L  | S  | C  | A  | A    | S  | G  | F  | T  | F  | S  | S  | Y  | A  | M     | S  | -  | -  | -  | W | V | R | Q | A  | P  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |

[illegible]

| Antibody number | FW 1 |   |   |   |   |   |   |   |   |    | CDR 1 |    |    |     |    |    |    |    |    |    | FW 2 |    |    |    |    |    |    |   |   |   | CDR 2 |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |   |   |    |    |    |    |
|-----------------|------|---|---|---|---|---|---|---|---|----|-------|----|----|-----|----|----|----|----|----|----|------|----|----|----|----|----|----|---|---|---|-------|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|---|---|----|----|----|----|
|                 | 1    | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11    | 12 | 13 | 14  | 15 | 16 | 17 | 18 | 19 | 20 | 21   | 22 | 23 | 24 | 25 | 26 | 27 | a | b | c | d     | e | f | g | h | i | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | a | b | c | d | e | 52 | 53 | 54 | 55 |
| 1               | Q    | A | V | L | T | Q | P | P | S | -  | V     | S  | G  | A   | P  | G  | Q  | R  | V  | T  | I    | S  | C  | T  | G  | S  | T  | S | S | N | I     | - | - | - | G | A | G  | Y  | D  | V  | H  | W  | Y  | Q  | Q  | L  | P  | G  | T  | A  | P  | K  | L  | L  | I  | Y  | G  | N  | -  | - | - | N | N | R | P  | S  |    |    |
| 2               | Q    | S | V | L | T | Q | P | P | S | -  | V     | S  | V  | A   | P  | G  | K  | T  | A  | T  | I    | P  | C  | G  | G  | T  | N  | - | - | - | -     | - | - | - | I | G | N  | K  | N  | V  | A  | H  | W  | Y  | Q  | K  | P  | G  | Q  | A  | P  | V  | L  | V  | I  | Y  | G  | D  | -  | - | - | S | D | R | P  | S  |    |    |
| 3               | S    | S | E | L | T | Q | D | P | A | -  | V     | S  | V  | A   | L  | G  | Q  | T  | V  | A  | I    | I  | P  | C  | R  | G  | D  | S | - | - | -     | - | - | - | - | I | L  | R  | M  | F  | A  | T  | W  | F  | Q  | K  | P  | G  | Q  | A  | P  | V  | L  | V  | I  | Y  | G  | D  | -  | - | - | T | Y | R | P  | S  |    |    |
| 4               | S    | Y | V | L | T | Q | P | P | S | -  | V     | S  | V  | S   | P  | G  | Q  | T  | A  | S  | I    | T  | C  | S  | G  | D  | K  | - | - | - | -     | - | - | - | - | L | G  | D  | K  | Y  | A  | S  | W  | Y  | Q  | K  | P  | G  | Q  | S  | P  | V  | L  | V  | I  | Y  | Q  | D  | -  | - | - | T | K | R | P  | S  |    |    |
| 5               | S    | Y | V | L | T | Q | P | P | S | -  | V     | S  | V  | S   | L  | G  | Q  | T  | A  | R  | I    | T  | C  | S  | G  | D  | A  | - | - | - | -     | - | - | - | - | L | P  | K  | Q  | Y  | A  | Y  | W  | Y  | Q  | K  | P  | G  | Q  | A  | P  | V  | L  | V  | I  | Y  | K  | D  | -  | - | - | S | E | R | P  | S  |    |    |
| 6               | D    | I | V | M | T | Q | S | P | S | T  | L     | S  | A  | S   | I  | G  | D  | R  | V  | T  | I    | I  | C  | R  | A  | S  | Q  | - | - | - | -     | - | - | - | - | G | I  | S  | S  | W  | L  | A  | W  | Y  | Q  | K  | P  | G  | R  | A  | P  | K  | V  | L  | I  | Y  | K  | A  | -  | - | - | S | T | L | E  | S  |    |    |
| 7               | D    | I | V | M | T | Q | S | P | S | T  | L     | S  | A  | S   | V  | G  | D  | R  | V  | T  | I    | I  | T  | C  | R  | A  | S  | Q | - | - | -     | - | - | - | - | - | G  | I  | S  | S  | W  | L  | A  | W  | Y  | Q  | K  | P  | G  | R  | A  | P  | K  | V  | L  | I  | Y  | K  | A  | - | - | - | S | T | L  | E  | S  |    |
| 8               | S    | Y | E | L | T | Q | P | P | S | -  | V     | S  | V  | P   | G  | Q  | T  | A  | T  | I  | T    | C  | S  | G  | D  | K  | -  | - | - | - | -     | - | - | - | - | L | D  | D  | K  | Y  | I  | S  | W  | Y  | Q  | R  | K  | P  | G  | Q  | A  | P  | V  | L  | L  | I  | Y  | Q  | D  | - | - | - | I | E | R  | P  | S  |    |
| 9               | Q    | S | V | V | T | Q | P | P | S | -  | A     | S  | G  | T   | P  | G  | Q  | R  | V  | T  | I    | I  | S  | C  | S  | G  | S  | S | S | N | -     | - | - | - | - | - | I  | G  | N  | N  | F  | V  | Q  | W  | Y  | Q  | L  | P  | G  | A  | P  | V  | L  | L  | I  | M  | N  | D  | -  | - | - | K | T | R | P  | S  |    |    |
| 10              | Q    | S | V | V | T | Q | P | P | S | -  | V     | S  | A  | A   | P  | G  | Q  | K  | V  | T  | I    | S  | C  | S  | G  | S  | S  | S | N | - | -     | - | - | - | - | - | I  | G  | N  | N  | V  | V  | S  | W  | Y  | Q  | L  | P  | G  | T  | A  | P  | K  | L  | L  | I  | Y  | D  | N  | - | - | - | N | K | R  | P  | S  |    |
| 11              | S    | Y | E | L | A | Q | P | P | S | -  | V     | S  | V  | S</ |    |    |    |    |    |    |      |    |    |    |    |    |    |   |   |   |       |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |   |   |    |    |    |    |

| Antibody number | FW 3 |    |    |    |    |    |    |    |    |    |    |    |   |   |    |    | CDR 3 |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | FW 4 |    |    |    |    |    |    |    |    |   |   |   |   |   |   |   |   |   |    |    |    |    |     |     |     |     |     |     |     |   |   |   |
|-----------------|------|----|----|----|----|----|----|----|----|----|----|----|---|---|----|----|-------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|------|----|----|----|----|----|----|----|----|---|---|---|---|---|---|---|---|---|----|----|----|----|-----|-----|-----|-----|-----|-----|-----|---|---|---|
|                 | 57   | 58 | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 | 67 | 68 | a | b | 69 | 70 | 71    | 72 | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 | 81 | 82 | 83 | 84 | 85 | 86 | 87   | 88 | 89 | 90 | 91 | 92 | 93 | 94 | 95 | a | b | c | d | e | f | g | h | i | 96 | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 | 105 | 106 | a | b | c |
| 1               | G    | V  | P  | D  | R  | F  | S  | G  | S  | K  | S  | G  | - | - | I  | S  | A     | S  | L  | A  | I  | T  | G  | L  | Q  | A  | E  | D  | E  | A  | D  | Y  | C    | D  | Y  | C  | Q  | S  | Y  | D  | I  | N | L | - | - | - | - | - | - | - | K  | V  | F  | G  | G   | G   | I   | K   | L   | I   | V   | - | - | L |
| 2               | G    | I  | P  | E  | R  | L  | S  | G  | S  | N  | S  | E  | - | - | N  | T  | A     | T  | L  | T  | I  | S  | R  | V  | E  | A  | G  | D  | E  | A  | D  | Y  | C    | Q  | V  | W  | D  | M  | T  | I  | D  | H | - | - | - | - | - | - | W | V | F  | G  | G  | T  | K   | L   | T   | V   | -   | -   | L   |   |   |   |
| 3               | G    | I  | P  | E  | R  | F  | S  | G  | S  | D  | S  | G  | - | - | D  | T  | A     | T  | L  | T  | I  | T  | G  | A  | Q  | A  | E  | D  | E  | A  | D  | Y  | C    | N  | S  | R  | D  | S  | T  | G  | N  | P | - | - | - | - | - | V | L | F | G  | G  | T  | K  | L   | T   | V   | -   | -   | L   |     |   |   |   |
| 4               | G    | I  | P  | E  | R  | F  | S  | G  | S  | N  | S  | G  | - | - | N  | I  | A     | T  | L  | I  | I  | S  | G  | I  | Q  | A  | L  | D  | E  | A  | D  | Y  | C    | Q  | A  | W  | D  | S  | S  | I  | A  | - | - | - | - | - | W | V | F | G | G  | I  | K  | L  | I   | V   | -   | -   | L   |     |     |   |   |   |
| 5               | G    | I  | P  | E  | R  | F  | S  | G  | S  | S  | S  | G  | - | - | I  | T  | V     | T  | L  | I  | I  | S  | G  | V  | Q  | A  | E  | D  | E  | A  | D  | Y  | C    | Q  | A  | D  | S  | S  | G  | I  | Y  | - | - | - | - | - | V | V | F | G | G  | I  | K  | L  | I   | V   | -   | -   | L   |     |     |   |   |   |
| 6               | G    | V  | P  | S  | R  | F  | S  | G  | S  | G  | S  | G  | - | - | T  | D  | F     | T  | L  | T  | I  | S  | S  | L  | Q  | P  | E  | D  | F  | A  | T  | Y  | C    | Q  | Q  | S  | Y  | S  | T  | P  | -  | - | - | - | - | W | T | F | G | Q | G  | T  | K  | L  | E   | I   | -   | -   | K   |     |     |   |   |   |
| 7               | G    | V  | P  | S  | R  | F  | S  | G  | S  | G  | S  | G  | - | - | T  | D  | F     | T  | L  | T  | I  | S  | S  | L  | Q  | P  | E  | D  | F  | A  | T  | Y  | C    | Q  | Q  | S  | Y  | S  | T  | P  | -  | - | - | - | - | W | T | F | G | Q | G  | T  | K  | L  | E   | I   | -   | -   | K   |     |     |   |   |   |
| 8               | G    | I  | P  | D  | R  | F  | S  | G  | S  | N  | S  | G  | - | - | N  | T  | A     | T  | L  | S  | I  | S  | G  | T  | Q  | S  | M  | D  | E  | A  | E  | Y  | C    | Q  | A  | W  | D  | S  | G  | A  | -  | - | - | - | - | I | V | F | G | G | T  | K  | L  | I  | V   | -   | -   | L   |     |     |     |   |   |   |
| 9               | A    | V  | P  | D  | R  | F  | S  | G  | S  | K  | S  | G  | - | - | T  | S  | A     | T  | L  | T  | I  | S  | G  | L  | R  | S  | E  | D  | E  | A  | D  | Y  | C    | A  | A  | W  | D  | D  | G  | L  | S  | G | - | - | - | - | P | V | F | G | G  | T  | K  | L  | I   | V   | -   | -   | L   |     |     |   |   |   |
| 10              | G    | I  | P  | D  | R  | F  | S  | G  | S  | K  | S  | G  | - | - | T  | S  | A     | T  | L  | G  | I  | T  | G  | L  | Q  | T  | S  | E  | D  | E  | A  | D  | Y    | C  | G  | T  | A  | D  | S  | S  | L  | S | A | - | - | - | - | G | V | F | G  | G  | T  | K  | L   | I   | V   | -   | -   | L   |     |   |   |   |
| 11              | G    | I  | P  | E  | R  | F  | S  | G  | S  | G  | S  | G  | - | - | I  | T  | V     | T  | L  | I  | I  | S  | G  | V  | Q  | A  | E  | D  | E  | A  | D  | Y  | C    | Q  | S  | A  | D  | S  | S  | G  | I  | Y | - | - | - | - | V | V | F | G | G  | I  | K  | V  | I   | V   | -   | -   | L   |     |     |   |   |   |
| 12              | G    | I  | P  | D  | R  | F  | S  | G  | S  | D  | S  | G  | - | - | N  | T  | A     | S  | L  | T  | I  | T  | G  | A  | Q  | A  | E  | D  | E  | A  |    |    |      |    |    |    |    |    |    |    |    |   |   |   |   |   |   |   |   |   |    |    |    |    |     |     |     |     |     |     |     |   |   |   |

**Figure 3: Antibodies (Abs) Binding and Function: Phage display P2X4 binding antibodies**

| Antibody number | Human P2X4 binding | Cynomologus P2X4 binding | Mouse P2X4 binding | Fraction of control at Human P2X4 | Fraction of control at Cyno P2X4 | Fraction of control at Mouse P2X4 | Concentration in Human ephys assay (mg/ml) | Concentration in Cyno ephys assay (mg/ml) | Concentration in Mouse ephys assay (mg/ml) |
|-----------------|--------------------|--------------------------|--------------------|-----------------------------------|----------------------------------|-----------------------------------|--------------------------------------------|-------------------------------------------|--------------------------------------------|
| 1               | +                  | +                        |                    | 4.01                              | 5.80                             | NT                                | 2.1                                        | 2.1                                       |                                            |
| 2               | +                  |                          |                    | 1.27                              | NT                               | NT                                | 1                                          |                                           |                                            |
| 3               | +                  |                          |                    | 2.08                              | NT                               | 1.39                              | 1                                          |                                           | 1.0                                        |
| 4               | +                  |                          |                    | 1.17                              | NT                               | NT                                | 1.6                                        |                                           |                                            |
| 5               | +                  | -                        |                    | 0.80                              | 0.89                             | NT                                | 1.3                                        | 1.3                                       |                                            |
| 6               | +                  |                          |                    | 1.35                              | NT                               | NT                                | 1                                          |                                           |                                            |
| 7               | +                  |                          |                    | 1.20                              | 1.11                             | NT                                | 3.3                                        |                                           |                                            |
| 8               | +                  | -                        |                    | 0.52                              | 1.03                             | NT                                | 1.46                                       | 1.5                                       |                                            |
| 9               | +                  |                          | +                  | 1.52                              | NT                               | 1.12                              | 1.75                                       |                                           | 1.0                                        |
| 10              | +                  |                          |                    | 1.21                              | NT                               | NT                                | 1                                          |                                           |                                            |
| 11              | +                  | -                        |                    | 0.01                              | 1.06                             | 1.11                              | 1.23                                       | 2.1                                       | 1.0                                        |
| 12              | +                  |                          |                    | 2.06                              | NT                               | NT                                | 0.11                                       |                                           |                                            |
| 13              | +                  |                          |                    | 1.18                              | NT                               | NT                                | 0.05                                       |                                           |                                            |
| 14              | +                  |                          |                    | 0.84                              | NT                               | NT                                | 0.25                                       |                                           |                                            |
| 15              | +                  |                          |                    | 2.89                              | NT                               | NT                                | 0.18                                       |                                           |                                            |
| 16              | +                  |                          |                    | 1.00                              | NT                               | NT                                | 0.1                                        |                                           |                                            |
| 17              | +                  |                          |                    | 1.09                              | NT                               | NT                                | 0.27                                       |                                           |                                            |
| 18              | +                  | +                        |                    | 0.57                              | 0.62                             | NT                                | 3.3                                        | 3.3                                       |                                            |
| 19              | +                  |                          |                    | 1.20                              | NT                               | NT                                | 0.13                                       |                                           |                                            |
| 20              | +                  |                          |                    | 1.38                              | NT                               | NT                                | 0.1                                        |                                           |                                            |
| 21              | +                  |                          |                    | 2.04                              | NT                               | NT                                | 0.49                                       |                                           |                                            |
| 22              | +                  |                          |                    | 1.31                              | NT                               | NT                                | 0.5                                        |                                           |                                            |
| 23              | +                  |                          |                    | 1.63                              | NT                               | NT                                | 0.54                                       |                                           |                                            |
| 24              | +                  | +                        | +                  | 1.69                              | NT                               | 1.76                              | 0.53                                       |                                           | 0.53                                       |
| 25              | -                  |                          | +                  | NT                                | NT                               | 0.96                              |                                            |                                           | 0.59                                       |
| 26              | +                  |                          |                    | 1.31                              | NT                               | NT                                | 0.61                                       |                                           |                                            |
| 27              | +                  |                          |                    | 1.02                              | NT                               | NT                                | 0.39                                       |                                           |                                            |

| Antibody number | Human P2X4 binding | Cynomologus P2X4 binding | Mouse P2X4 binding | Fraction of control at Human P2X4 | Fraction of control at Cyno P2X4 | Fraction of control at Mouse P2X4 | Concentration in Human ephys assay (mg/ml) | Concentration in Cyno ephys assay (mg/ml) | Concentration in Mouse ephys assay (mg/ml) |
|-----------------|--------------------|--------------------------|--------------------|-----------------------------------|----------------------------------|-----------------------------------|--------------------------------------------|-------------------------------------------|--------------------------------------------|
| 28              | +                  | +                        |                    | 1.41                              | NT                               | NT                                | 0.56                                       |                                           |                                            |
| 29              | +                  | -                        |                    | 0.27                              | 1.11                             | NT                                | 4.2                                        | 1.1                                       |                                            |
| 30              | +                  |                          |                    | 1.28                              | NT                               | NT                                | 0.63                                       |                                           |                                            |
| 31              | +                  |                          |                    | 2.41                              | NT                               | 1.37                              | 0.35                                       |                                           | 0.33                                       |
| 32              | +                  |                          |                    | 0.84                              | NT                               | 1.04                              | 0.61                                       |                                           | 0.61                                       |
| 33              | +                  | -                        |                    | 0.62                              | 0.95                             | NT                                | 3.8                                        | 3.8                                       |                                            |
| 34              | +                  | +                        | +                  | 1.10                              | NT                               | NT                                | 1.16                                       |                                           |                                            |

| Key   |                                   |
|-------|-----------------------------------|
| +     | Binding observed in FMAT assay    |
| -     | No binding observed in FMAT assay |
| NT    | Not tested in assay               |
| blank | Data not disclosed                |

**Figure 4: Lead Panel Ephys**

| Antibody number | Conc (mg/ml) | Fraction of control at human P2X4 |       |    | Fraction of control at cyno P2X4 |       |    |
|-----------------|--------------|-----------------------------------|-------|----|----------------------------------|-------|----|
|                 |              | Mean                              | SEM   | n  | Mean                             | SEM   | n  |
| 5               | 1.3          | 0.74                              | 0.037 | 7  |                                  |       |    |
| 8               | 1.5          | 0.53                              | 0.011 | 8  |                                  |       |    |
| 11              | 2            | 0.03                              | 0.031 | 7  |                                  |       |    |
| 18              | 3.3          | 0.56                              | 0.010 | 6  | 0.62                             | 0.009 | 11 |
| 29              | 4.2          | 0.27                              | 0.013 | 18 |                                  |       |    |
| 33              | 3.8          | 0.62                              | 0.024 | 4  |                                  |       |    |

**Figure 5: Summary of human cross reactive hybridoma antibodies (Abs)**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Concentration ( $\mu$ M) | Fraction of control at Mouse P2X4 | Fraction of control at p2X4 (repeat | N | SD    | Concentration ( $\mu$ M) | Fraction of control at Human P2X4 | N | SD    |
|-----------------|--------------------|-------------------------|--------------------|--------------------------|-----------------------------------|-------------------------------------|---|-------|--------------------------|-----------------------------------|---|-------|
| 35              | +                  |                         | +                  | 0.80                     | 0.461                             | 0.194                               | 3 | 0.157 | 0.689                    | 0.648                             | 3 | 0.120 |
| 36              | +                  |                         | +                  | 2.18                     | 0.051                             | 0.045                               | 3 | 0.018 | 2.067                    | 0.604                             | 2 | 0.207 |
| 37              | +                  |                         | +                  | 1.38                     | 0.270                             | 0.242                               | 4 | 0.068 | 2.200                    | 1.056                             | 3 | 0.139 |
| 38              | +                  |                         | +                  | 0.269                    | 0.178                             | 0.157                               | 3 | 0.021 | 0.733                    | 0.486                             | 2 | 0.085 |
| 39              | +                  |                         | +                  | 0.941                    | -0.067                            | 0.068                               | 3 | 0.074 |                          | NT                                |   |       |
| 40              | +                  |                         | +                  | 1.17                     | 0.231                             | 0.191                               | 2 | 0.018 | 1.711                    | 0.815                             | 3 | 0.178 |
| 41              | +                  |                         | +                  | 0.49                     | 0.072                             | 0.195                               | 4 | 0.033 | 0.378                    | 0.633                             | 4 | 0.103 |
| 42              | +                  |                         | +                  | 0.724                    | 0.333                             | 0.193                               | 3 | 0.075 | 1.089                    | 0.414                             | 3 | 0.071 |
| 43              | +                  | +                       | +                  | 0.571                    | 0.307                             | 0.342                               | 3 | 0.060 | 2.044                    | 0.395                             | 3 | 0.058 |
| 44              | +                  |                         | +                  | 0.23                     | 0.253                             | 0.364                               | 4 | 0.107 |                          | NT                                |   |       |
| 45              | +                  |                         | +                  | 1.05                     | 0.281                             | 0.298                               | 1 |       | 1.844                    | 0.620                             | 3 | 0.140 |
| 46              | +                  |                         | +                  | 2.64                     | -0.079                            | -0.053                              | 4 | 0.095 | 1.622                    | 0.383                             | 2 | 0.036 |
| 47              | +                  |                         | +                  | 1.07                     | 0.196                             | 0.174                               | 3 | 0.089 | 0.311                    | 0.912                             | 3 | 0.112 |
| 48              | +                  |                         | +                  | 1.51                     | 0.041                             | 0.019                               | 3 | 0.076 | 1.956                    | 0.560                             | 3 | 0.096 |

| Key         | Description                       |
|-------------|-----------------------------------|
| +           | Binding observed in FMAT assay    |
| -           | No binding observed in FMAT assay |
| Blank or NT | Data not disclosed / not tested   |

**Figure 6 part 1: Hybridoma derived P2X4 Antibodies (Abs) VH sequences**

| Antibody number | FW 1 |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | CDR 1 |    |    |    |    |   |   |   |   |  |
|-----------------|------|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|-------|----|----|----|----|---|---|---|---|--|
| Kabat numbering | 1    | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31    | 32 | 33 | 34 | 35 | a | b | c | d |  |
| 35              | E    | I | Q | L | Q | E | S | G | P | G  | L  | V  | K  | P  | S  | Q  | S  | L  | S  | L  | T  | C  | S  | V  | T  | G  | Y  | T  | I  | T  | S     | G  | Y  | D  | -  | - | - | - |   |  |
| 36              | Q    | V | Q | L | K | E | S | G | P | G  | L  | V  | K  | P  | S  | E  | T  | L  | S  | L  | T  | C  | T  | V  | S  | G  | F  | S  | L  | T  | N     | Y  | H  | V  | N  | - | - | - | - |  |
| 37              | Q    | V | N | L | L | Q | S | G | A | A  | L  | V  | K  | P  | G  | A  | S  | V  | K  | L  | S  | C  | K  | A  | S  | G  | Y  | T  | F  | T  | D     | Y  | Y  | I  | H  | - | - | - | - |  |
| 38              | E    | I | Q | L | Q | E | S | G | P | G  | L  | V  | K  | P  | S  | Q  | S  | L  | S  | L  | T  | C  | S  | V  | T  | G  | Y  | T  | I  | T  | S     | G  | Y  | D  | -  | - | - | - |   |  |
| 39              | E    | I | Q | L | Q | E | S | G | P | G  | L  | V  | K  | P  | S  | Q  | S  | L  | S  | L  | T  | C  | S  | V  | T  | G  | Y  | T  | I  | T  | S     | G  | S  | D  | -  | - | - | - |   |  |
| 40              | Q    | V | T | L | K | E | S | G | P | G  | I  | L  | Q  | P  | S  | Q  | T  | L  | S  | L  | T  | C  | S  | F  | S  | G  | F  | S  | L  | S  | T     | F  | G  | I  | C  | V | S | - | - |  |
| 41              | Q    | V | Q | L | K | E | S | G | P | G  | L  | V  | K  | P  | S  | E  | T  | L  | S  | L  | T  | C  | T  | V  | S  | G  | F  | S  | L  | T  | S     | Y  | H  | V  | R  | - | - | - | - |  |
| 42              | E    | I | Q | L | Q | E | S | G | P | G  | L  | V  | K  | P  | S  | Q  | S  | L  | S  | L  | T  | C  | S  | V  | T  | G  | Y  | T  | I  | T  | S     | G  | Y  | D  | -  | - | - | - |   |  |
| 43              | Q    | V | Q | L | K | E | S | G | P | G  | L  | V  | Q  | P  | S  | Q  | T  | L  | S  | L  | T  | C  | T  | V  | S  | G  | F  | S  | L  | T  | R     | Y  | D  | V  | H  | - | - | - | - |  |
| 44              | Q    | V | T | L | K | E | S | G | P | G  | I  | L  | Q  | P  | S  | Q  | T  | L  | S  | L  | T  | C  | S  | F  | S  | G  | F  | S  | L  | N  | T     | Y  | G  | I  | C  | V | S | - | - |  |
| 45              | E    | I | Q | L | Q | E | S | G | P | G  | L  | V  | K  | P  | S  | Q  | S  | L  | S  | L  | T  | C  | S  | V  | T  | G  | Y  | T  | I  | T  | S     | G  | F  | D  | -  | - | - | - |   |  |
| 46              | Q    | V | Q | L | K | E | S | G | P | G  | L  | V  | K  | P  | S  | E  | T  | L  | S  | L  | T  | C  | T  | V  | S  | G  | F  | S  | L  | T  | S     | Y  | H  | V  | S  | - | - | - | - |  |
| 47              | E    | I | Q | L | Q | E | S | G | P | G  | L  | V  | K  | P  | S  | Q  | S  | L  | S  | L  | T  | C  | S  | V  | T  | G  | Y  | T  | I  | T  | S     | G  | F  | D  | -  | - | - | - |   |  |
| 48              | Q    | V | Q | L | K | E | S | G | P | G  | L  | V  | K  | P  | S  | E  | T  | L  | S  | L  | T  | C  | T  | V  | S  | G  | F  | S  | L  | T  | S     | Y  | H  | V  | S  | - | - | - | - |  |

**Figure 6 part 2: Hybridoma derived P2X4 Antibodies (Abs) VH sequences**

| Antibody number | FW 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | CDR 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------|------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Kabat numbering |      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

[illegible]

**Figure 6 part 4: Hybridoma derived P2X4 Antibodies (Abs) VH sequences**

| Antibody number | FW 4 |     |     |     |     |     |     |     |     |     |     |  |
|-----------------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Kabat numbering | 103  | 104 | 105 | 106 | 107 | 108 | 109 | 110 | 111 | 112 | 113 |  |
| 35              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 36              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 37              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 38              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 39              | W    | G   | R   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 40              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 41              | W    | G   | Q   | G   | T   | L   | V   | T   | V   | S   | S   |  |
| 42              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 43              | W    | G   | Q   | G   | T   | L   | V   | T   | V   | S   | S   |  |
| 44              | W    | G   | Q   | G   | V   | M   | V   | T   | V   | S   | S   |  |
| 45              | W    | G   | Q   | G   | T   | L   | V   | T   | V   | S   | S   |  |
| 46              | W    | G   | Q   | G   | T   | L   | V   | T   | V   | S   | S   |  |
| 47              | W    | G   | Q   | G   | T   | L   | V   | T   | V   | S   | S   |  |
| 48              | W    | G   | Q   | G   | T   | L   | V   | T   | V   | S   | S   |  |

**Figure 6 part 5: Hybridoma derived P2X4 Antibodies (Abs) VL sequences**

| Antibody number | FW 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | CDR 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------|------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                 |      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**Figure 6 part 6: Hybridoma derived P2X4 Antibodies (Abs) VL sequences**

| Antibody number |    | FW 2 |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | CDR 2 |   |   |   |   |   |    |    |    |    |    |  |
|-----------------|----|------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|-------|---|---|---|---|---|----|----|----|----|----|--|
| Kabat numbering |    | 35   | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 51    | a | b | c | d | e | 52 | 53 | 54 | 55 | 56 |  |
|                 | 35 | W    | Y  | H  | Q  | K  | P  | G  | E  | P  | Y  | N  | L  | L  | I  | Y  | S  | G     | - | - | - | - | - | S  | T  | L  | Q  | S  |  |
|                 | 36 | W    | Y  | Q  | Q  | K  | P  | G  | K  | S  | P  | Q  | L  | L  | I  | Y  | D  | A     | - | - | - | - | T | S  | L  | A  | D  |    |  |
|                 | 37 | W    | Y  | Q  | Q  | K  | S  | G  | A  | S  | P  | K  | P  | W  | I  | Y  | E  | T     | - | - | - | - | S | K  | L  | A  | S  |    |  |
|                 | 38 | W    | Y  | Q  | Q  | K  | P  | G  | E  | A  | F  | K  | L  | L  | I  | Y  | S  | G     | - | - | - | - | S | T  | L  | Q  | S  |    |  |
|                 | 39 | W    | Y  | Q  | Q  | K  | P  | G  | E  | A  | N  | K  | L  | L  | I  | Y  | S  | G     | - | - | - | - | S | T  | L  | Q  | S  |    |  |
|                 | 40 | W    | F  | Q  | Q  | K  | P  | G  | K  | S  | P  | Q  | L  | L  | I  | Y  | D  | A     | - | - | - | - | T | T  | L  | A  | D  |    |  |
|                 | 41 | W    | Y  | Q  | Q  | K  | P  | G  | K  | S  | P  | Q  | L  | L  | L  | Y  | D  | A     | - | - | - | - | T | S  | L  | A  | D  |    |  |
|                 | 42 | W    | Y  | Q  | Q  | K  | P  | G  | E  | A  | Y  | K  | L  | L  | I  | Y  | S  | G     | - | - | - | - | S | T  | L  | Q  | S  |    |  |
|                 | 43 | W    | Y  | Q  | Q  | K  | P  | G  | K  | A  | P  | R  | Q  | L  | I  | R  | Y  | T     | - | - | - | - | S | A  | L  | V  | S  |    |  |
|                 | 44 | W    | Y  | Q  | Q  | K  | P  | G  | K  | S  | P  | Q  | L  | L  | I  | Y  | D  | A     | - | - | - | - | T | S  | L  | A  | D  |    |  |
|                 | 45 | W    | Y  | Q  | Q  | K  | P  | G  | E  | P  | Y  | N  | L  | L  | I  | Y  | S  | G     | - | - | - | - | S | T  | L  | Q  | S  |    |  |
|                 | 46 | W    | Y  | Q  | Q  | K  | P  | G  | K  | S  | P  | Q  | L  | L  | I  | Y  | D  | A     | - | - | - | - | T | T  | L  | A  | D  |    |  |
|                 | 47 | W    | Y  | Q  | Q  | K  | P  | G  | E  | P  | Y  | N  | L  | L  | I  | H  | S  | G     | - | - | - | - | S | T  | L  | Q  | S  |    |  |
|                 | 48 | W    | Y  | Q  | Q  | K  | P  | G  | K  | S  | P  | H  | L  | L  | I  | Y  | D  | A     | - | - | - | - | T | T  | L  | A  | D  |    |  |

**Figure 6 part 7: Hybridoma derived P2X4 Antibodies (Abs) VL sequences**

| Antibody number |  | FW 3 |    |    |    |    |    |    |    |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | CDR 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | WO 2015/166105 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------|--|------|----|----|----|----|----|----|----|----|----|----|----|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Kabat numbering |  | 57   | 58 | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 | 67 | 68 | a | 69 | 70 | 71 | 72 | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 | 81 | 82 | 83 | 84 | 85 | 86 | 87 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |                |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

WO 2015/166105

PCT/EP2015/059633

**Figure 6 part 8: Hybridoma derived P2X4 Antibodies (Abs) VL sequences**

| Antibody number | FW 4 |    |     |     |     |     |     |     |     |   |   |   |     |
|-----------------|------|----|-----|-----|-----|-----|-----|-----|-----|---|---|---|-----|
| Kabat numbering | 98   | 99 | 100 | 101 | 102 | 103 | 104 | 105 | 106 | a | b | c | 107 |
| 35              | F    | G  | A   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 36              | F    | G  | G   | G   | S   | K   | L   | E   | L   | - | - | - | K   |
| 37              | F    | G  | G   | G   | T   | K   | L   | E   | M   | - | - | - | R   |
| 38              | F    | G  | A   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 39              | F    | G  | S   | G   | T   | K   | L   | E   | I   | - | - | - | K   |
| 40              | F    | G  | P   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 41              | F    | G  | G   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 42              | F    | G  | A   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 43              | F    | G  | A   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 44              | F    | G  | S   | G   | T   | K   | L   | E   | I   | - | - | - | K   |
| 45              | F    | G  | A   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 46              | F    | G  | G   | G   | T   | N   | L   | E   | L   | - | - | - | K   |
| 47              | F    | G  | A   | G   | T   | K   | L   | E   | L   | - | - | - | K   |
| 48              | F    | G  | G   | G   | T   | K   | L   | E   | L   | - | - | - | K   |

**Figure 7: Part 1a - Antibodies (Abs) Binding and Function: Hybridoma P2X4 binding antibodies (all clones)**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (µg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 35              | +                  |                         | +                  | 0.648                                             | 0.461                                             | 119                                  |
| 36              | +                  | -                       | +                  | 0.604                                             | 0.051                                             | 327                                  |
| 37              | +                  |                         | +                  | 1.056                                             | 0.270                                             | 207                                  |
| 38              | +                  | -                       | +                  | 0.486                                             | 0.178                                             | 40                                   |
| 39              | +                  | -                       | +                  |                                                   | -0.067                                            | 141                                  |
| 40              | +                  |                         | +                  | 0.815                                             | 0.231                                             | 176                                  |
| 41              | +                  |                         | +                  | 0.633                                             | 0.072                                             | 73                                   |
| 42              | +                  |                         | +                  | 0.414                                             | 0.333                                             | 109                                  |
| 43              | +                  | +                       | +                  | 0.395                                             | 0.307                                             | 86                                   |
| 44              | +                  |                         | +                  |                                                   | 0.253                                             | 35                                   |
| 45              | +                  |                         | +                  | 0.620                                             | 0.281                                             | 158                                  |
| 46              | +                  | -                       | +                  | 0.383                                             | -0.079                                            | 396                                  |
| 47              | +                  | -                       | +                  | 0.912                                             | 0.196                                             | 161                                  |
| 48              | +                  | -                       | +                  | 0.560                                             | 0.041                                             | 227                                  |
| 49              |                    |                         | +                  |                                                   | 0.940                                             | 53                                   |
| 50              |                    |                         | +                  |                                                   | 0.584                                             | 246                                  |
| 51              |                    |                         | +                  |                                                   | 0.516                                             | 57                                   |
| 52              |                    |                         | +                  |                                                   | 0.569                                             | 81                                   |
| 53              |                    |                         | +                  |                                                   | 3.187                                             | 113                                  |
| 54              |                    |                         | +                  |                                                   | 0.570                                             | 104                                  |
| 55              |                    |                         | +                  |                                                   | 0.607                                             | 86                                   |
| 56              |                    |                         | +                  |                                                   | 1.080                                             | 113                                  |
| 57              |                    |                         | +                  |                                                   | 0.651                                             | <LOD                                 |
| 58              |                    |                         | +                  |                                                   | 0.486                                             | 179                                  |
| 59              |                    |                         | +                  |                                                   | 1.093                                             | 83                                   |
| 60              |                    |                         | +                  |                                                   | 1.733                                             | <LOD                                 |
| 61              | +                  |                         | +                  |                                                   | 0.115                                             | 24                                   |
| 62              |                    |                         | +                  |                                                   | 1.177                                             | 20                                   |

| Key         |                                   |
|-------------|-----------------------------------|
| +           | Binding observed in FMAT assay    |
| -           | No binding observed in FMAT assay |
| NT or Blank | Not tested in assay               |
| < LOD       | [IgG] below limit of detection    |

**Figure 7: Part 1b**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (µg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 63              |                    |                         | +                  |                                                   | 0.976                                             | <LOD                                 |
| 64              |                    |                         | +                  |                                                   | 1.893                                             | 67                                   |
| 65              | -                  | -                       | +                  |                                                   | 0.394                                             | 364                                  |
| 66              |                    |                         | +                  |                                                   | 1.574                                             | 85                                   |
| 67              |                    |                         | +                  |                                                   | 0.714                                             | 107                                  |
| 68              |                    |                         | +                  |                                                   | 1.767                                             | 107                                  |
| 69              |                    |                         | +                  |                                                   | 0.887                                             | 89                                   |
| 70              |                    |                         | +                  |                                                   | 0.794                                             | 161                                  |
| 71              |                    |                         | +                  |                                                   | 3.280                                             | 76                                   |
| 72              |                    |                         | +                  |                                                   | 0.662                                             | 337                                  |
| 73              |                    |                         | +                  |                                                   | 0.467                                             | 71                                   |
| 74              |                    |                         | +                  |                                                   | 3.767                                             | 95                                   |
| 75              |                    |                         | +                  |                                                   | 0.713                                             | 61                                   |
| 76              |                    |                         | +                  |                                                   | 0.793                                             | 91                                   |
| 77              |                    |                         | +                  |                                                   | 1.118                                             | 37                                   |
| 78              |                    |                         | +                  |                                                   | 0.763                                             | 54                                   |
| 79              |                    |                         | +                  |                                                   | 0.686                                             | 38                                   |
| 80              |                    |                         | +                  |                                                   | 0.650                                             | <LOD                                 |
| 81              |                    |                         | +                  |                                                   | 0.832                                             | 199                                  |
| 82              |                    |                         | +                  |                                                   | 1.240                                             | 181                                  |
| 83              |                    |                         | +                  |                                                   | 1.091                                             | 372                                  |
| 84              |                    |                         | +                  |                                                   | 0.381                                             | 31                                   |
| 85              |                    |                         | +                  |                                                   | 1.821                                             | <LOD                                 |
| 86              |                    |                         | +                  |                                                   | 1.153                                             | <LOD                                 |
| 87              |                    |                         | +                  |                                                   | 0.760                                             | 212                                  |
| 88              |                    |                         | +                  |                                                   | 1.003                                             | 219                                  |

**Figure 7: Part 1c**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 89              |                    |                         | +                  |                                                   | 1.710                                             | 381                                  |
| 90              |                    |                         | +                  |                                                   | 0.533                                             | 210                                  |
| 91              |                    |                         | +                  |                                                   | 1.338                                             | 116                                  |
| 92              |                    |                         | +                  |                                                   | 2.653                                             | 80                                   |
| 93              |                    |                         | +                  |                                                   | 1.743                                             | 171                                  |
| 94              |                    |                         | +                  |                                                   | 2.033                                             | 136                                  |
| 95              |                    |                         | +                  |                                                   | 1.221                                             | 48                                   |
| 96              |                    |                         | +                  |                                                   | 0.539                                             | 89                                   |
| 97              |                    |                         | +                  |                                                   | 0.976                                             | 94                                   |
| 98              |                    |                         | +                  |                                                   | 0.564                                             | 69                                   |
| 99              |                    |                         | +                  |                                                   | 0.821                                             | 181                                  |
| 100             |                    |                         | +                  |                                                   | 0.907                                             | 30                                   |
| 101             |                    |                         | +                  |                                                   | 4.969                                             | 318                                  |
| 102             |                    |                         | +                  |                                                   | 0.778                                             | 321                                  |
| 103             |                    |                         | +                  |                                                   | 0.860                                             | 94                                   |
| 104             |                    |                         | +                  |                                                   | 0.720                                             | 311                                  |
| 105             |                    |                         | +                  |                                                   | 0.398                                             | 233                                  |
| 106             |                    |                         | +                  |                                                   | 0.703                                             | 233                                  |
| 107             | -                  |                         | +                  | 0.540                                             | 0.151                                             | 84                                   |
| 108             |                    |                         | +                  |                                                   | 1.007                                             | 258                                  |
| 109             |                    |                         | +                  |                                                   | 0.805                                             | 52                                   |
| 110             |                    |                         | +                  |                                                   | 0.780                                             | 89                                   |
| 111             |                    |                         | +                  |                                                   | 0.025                                             | 216                                  |
| 112             |                    |                         | +                  |                                                   | 0.650                                             | 86                                   |
| 113             |                    |                         | +                  |                                                   | 1.136                                             | 238                                  |
| 114             |                    |                         | +                  |                                                   | 1.567                                             | 398                                  |
| 115             |                    |                         | +                  |                                                   | 1.635                                             | 183                                  |

**Figure 7: Part 1d**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 115             |                    |                         | +                  |                                                   | 1.635                                             | 183                                  |
| 116             |                    |                         | +                  |                                                   | 1.287                                             | 141                                  |
| 117             |                    |                         | +                  |                                                   | 0.749                                             | 315                                  |
| 118             | -                  | -                       | +                  |                                                   | 0.398                                             | 103                                  |
| 119             |                    |                         | +                  |                                                   | 2.211                                             | 49                                   |
| 120             |                    |                         | +                  |                                                   | 0.845                                             | 317                                  |
| 121             |                    |                         | +                  |                                                   | 0.952                                             | 73                                   |
| 122             |                    |                         | +                  |                                                   | 0.982                                             | 103                                  |
| 123             |                    |                         | +                  |                                                   | 0.933                                             | 235                                  |
| 124             |                    |                         | +                  |                                                   | 0.711                                             | 120                                  |
| 125             |                    |                         | +                  |                                                   | 1.738                                             | 360                                  |
| 126             |                    |                         | +                  |                                                   | 1.792                                             | 106                                  |
| 127             |                    |                         | +                  |                                                   | 0.467                                             | 75                                   |
| 128             |                    |                         | +                  |                                                   | 0.542                                             | 76                                   |
| 129             |                    |                         | +                  |                                                   | 0.716                                             | 57                                   |
| 130             |                    |                         | +                  |                                                   | 0.595                                             | 138                                  |
| 131             |                    |                         | +                  |                                                   | 1.233                                             | 351                                  |
| 132             |                    |                         | +                  |                                                   | 0.560                                             | 118                                  |
| 133             |                    |                         | +                  |                                                   | 0.608                                             | 195                                  |
| 134             |                    |                         | +                  |                                                   | 1.455                                             | 97                                   |
| 135             |                    |                         | +                  |                                                   | 1.157                                             | 81                                   |
| 136             |                    |                         | +                  |                                                   | 0.679                                             | 70                                   |
| 137             |                    |                         | +                  |                                                   | 0.903                                             | 118                                  |
| 138             |                    |                         | +                  |                                                   | 1.521                                             | 295                                  |
| 139             |                    |                         | +                  |                                                   | 1.458                                             | 150                                  |
| 140             |                    |                         | +                  |                                                   | 0.573                                             | 118                                  |

**Figure 7: Part 1e**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 141             |                    |                         | +                  |                                                   | 0.892                                             | 231                                  |
| 142             |                    |                         | +                  |                                                   | 1.505                                             | 367                                  |
| 143             |                    |                         | +                  |                                                   | 0.770                                             | 269                                  |
| 144             |                    |                         | +                  |                                                   | 0.656                                             | 174                                  |
| 145             | -                  | +                       | +                  |                                                   | 0.150                                             | 69                                   |
| 146             |                    |                         | +                  |                                                   | 1.480                                             | 141                                  |
| 147             |                    |                         | +                  |                                                   | 0.727                                             | 60                                   |
| 148             |                    |                         | +                  |                                                   | 2.619                                             | 391                                  |
| 149             |                    |                         | +                  |                                                   | 1.602                                             | 379                                  |
| 150             |                    |                         | +                  |                                                   | 0.450                                             | 203                                  |
| 151             |                    |                         | +                  |                                                   | 1.011                                             | 293                                  |
| 152             |                    |                         | +                  |                                                   | 0.538                                             | 400                                  |
| 153             |                    |                         | +                  |                                                   | 1.928                                             | 282                                  |
| 154             |                    |                         | +                  |                                                   | 0.704                                             | 444                                  |
| 155             |                    |                         | +                  |                                                   | 0.928                                             | 279                                  |
| 156             |                    |                         | +                  |                                                   | 1.078                                             | <LOD                                 |
| 157             |                    |                         | +                  |                                                   | 1.036                                             | 247                                  |
| 158             |                    |                         | +                  |                                                   | 1.306                                             | 298                                  |
| 159             |                    |                         | +                  |                                                   | 5.781                                             | 118                                  |
| 160             |                    |                         | +                  |                                                   | 0.918                                             | 180                                  |
| 161             |                    |                         | +                  |                                                   | 0.956                                             | 206                                  |
| 162             |                    |                         | +                  |                                                   | 1.388                                             | 155                                  |
| 163             | -                  | -                       | +                  |                                                   | 0.375                                             | 59                                   |
| 164             |                    |                         | +                  |                                                   | 0.546                                             | 268                                  |
| 165             |                    |                         | +                  |                                                   | 0.616                                             | <LOD                                 |

**Figure 7: Part 1f**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 166             |                    |                         | +                  |                                                   | 0.810                                             | 182                                  |
| 167             |                    |                         | +                  |                                                   | 1.258                                             | 151                                  |
| 168             |                    |                         | +                  |                                                   | 1.808                                             | 88                                   |
| 169             |                    |                         | +                  |                                                   | 1.773                                             | 128                                  |
| 170             |                    |                         | +                  |                                                   | 0.690                                             | 93                                   |
| 171             |                    |                         | +                  |                                                   | 0.524                                             | 396                                  |
| 172             | -                  | -                       | +                  | 1.078                                             | 0.307                                             | 364                                  |
| 173             |                    |                         | +                  |                                                   | 0.702                                             | 154                                  |
| 174             |                    |                         | +                  |                                                   | 0.656                                             | 225                                  |
| 175             |                    |                         | +                  |                                                   | 1.223                                             | 286                                  |
| 176             |                    |                         | +                  |                                                   | 1.444                                             | 148                                  |
| 177             |                    |                         | +                  |                                                   | 0.728                                             | 251                                  |
| 178             |                    |                         | +                  |                                                   | 1.356                                             | 297                                  |
| 179             |                    |                         | +                  |                                                   | 0.988                                             | 332                                  |
| 180             |                    |                         | +                  |                                                   | 0.679                                             | 351                                  |
| 181             |                    |                         | +                  |                                                   | 1.392                                             | 89                                   |
| 182             |                    |                         | +                  |                                                   | 0.572                                             | <LOD                                 |
| 183             |                    |                         | +                  |                                                   | 0.627                                             | 193                                  |
| 184             |                    |                         | +                  |                                                   | 0.373                                             | 84                                   |
| 185             |                    |                         | +                  |                                                   | 0.484                                             | 310                                  |
| 186             |                    |                         | +                  |                                                   | 1.320                                             | 257                                  |
| 187             |                    |                         | +                  |                                                   | 0.846                                             | 315                                  |
| 188             |                    |                         | +                  |                                                   | 0.645                                             | 114                                  |
| 189             | +                  | -                       | +                  | 0.593                                             | 0.082                                             | 208                                  |
| 190             |                    |                         | +                  |                                                   | 0.505                                             | 127                                  |
| 191             |                    |                         | +                  |                                                   | 0.932                                             | 97                                   |
| 192             |                    |                         | +                  |                                                   | 1.855                                             | 29                                   |
| 193             |                    |                         | +                  |                                                   | 0.660                                             | <LOD                                 |
| 194             |                    |                         | +                  |                                                   | 0.940                                             | 225                                  |

**Figure 7: Part 1g**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 195             |                    |                         | +                  |                                                   | 0.896                                             | 110                                  |
| 196             |                    |                         | +                  |                                                   | 0.860                                             | 100                                  |
| 197             |                    |                         | +                  |                                                   | 0.666                                             | 155                                  |
| 198             |                    |                         | +                  |                                                   | 0.801                                             | 57                                   |
| 199             |                    |                         | +                  |                                                   | 0.650                                             | 413                                  |
| 200             |                    |                         | +                  |                                                   | 0.503                                             | 110                                  |
| 201             |                    |                         | +                  |                                                   | 0.584                                             | 124                                  |
| 202             |                    |                         | +                  |                                                   | 0.998                                             | 317                                  |
| 203             |                    |                         | +                  |                                                   | 0.690                                             | 283                                  |
| 204             |                    |                         | +                  |                                                   | 1.202                                             | 104                                  |
| 205             |                    |                         | +                  |                                                   | 0.707                                             | 279                                  |
| 206             |                    |                         | +                  |                                                   | 0.911                                             | 104                                  |
| 207             |                    |                         | +                  |                                                   | 0.629                                             | 324                                  |
| 208             | -                  | -                       | +                  | 0.937                                             | 0.072                                             | 296                                  |
| 209             |                    |                         | +                  |                                                   | 0.709                                             | 126                                  |
| 210             |                    |                         | +                  |                                                   | 1.506                                             | 411                                  |
| 211             |                    |                         | +                  |                                                   | 1.108                                             | 74                                   |
| 212             |                    |                         | +                  |                                                   | 1.031                                             | 91                                   |
| 213             |                    |                         | +                  |                                                   | 1.346                                             | 223                                  |
| 214             |                    |                         | +                  |                                                   | 0.873                                             | 85                                   |
| 215             |                    |                         | +                  |                                                   | 0.512                                             | 373                                  |
| 216             |                    |                         | +                  |                                                   | 1.177                                             | 124                                  |
| 217             |                    |                         | +                  |                                                   | 0.826                                             | 66                                   |
| 218             |                    |                         | +                  |                                                   | 0.711                                             | 73                                   |
| 219             |                    |                         | +                  |                                                   | 0.746                                             | 100                                  |
| 220             |                    |                         | +                  |                                                   | 0.645                                             | 139                                  |
| 221             | -                  | -                       | +                  | 1.009                                             | 0.163                                             | 363                                  |

**Figure 7: Part 1h**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 222             |                    |                         | +                  |                                                   | 1.317                                             | <LOD                                 |
| 223             |                    |                         | +                  |                                                   | 1.071                                             | 102                                  |
| 224             |                    |                         | +                  |                                                   | 1.047                                             | 337                                  |
| 225             |                    |                         | +                  |                                                   | 0.539                                             | 81                                   |
| 226             |                    |                         | +                  |                                                   | 0.914                                             | 207                                  |
| 227             |                    |                         | +                  |                                                   | 0.781                                             | 111                                  |
| 228             |                    |                         | +                  |                                                   | 0.946                                             | 92                                   |
| 229             |                    |                         | +                  |                                                   | 0.760                                             | 135                                  |
| 230             |                    |                         | +                  |                                                   | 1.131                                             | 117                                  |
| 231             |                    |                         | +                  |                                                   | 1.840                                             | 262                                  |
| 232             |                    |                         | +                  |                                                   | 0.652                                             | 281                                  |
| 233             |                    |                         | +                  |                                                   | 0.714                                             | 486                                  |
| 234             | -                  |                         | +                  | 0.807                                             | 0.156                                             | 452                                  |
| 235             |                    |                         | +                  |                                                   | 0.660                                             | 287                                  |
| 236             |                    |                         | +                  |                                                   | 0.530                                             | 58                                   |
| 237             |                    |                         | +                  |                                                   | 0.725                                             | 355                                  |
| 238             | -                  |                         | +                  | 0.968                                             | 0.238                                             | 157                                  |
| 239             |                    |                         | +                  |                                                   | 1.064                                             | <LOD                                 |
| 240             |                    |                         | +                  |                                                   | 1.899                                             | <LOD                                 |
| 241             |                    |                         | +                  |                                                   | 0.877                                             | <LOD                                 |
| 242             |                    |                         | +                  |                                                   | 1.059                                             | 230                                  |
| 243             |                    |                         | +                  |                                                   | 1.143                                             | 18                                   |
| 244             |                    |                         | +                  |                                                   | 0.787                                             | 171                                  |
| 245             |                    |                         | +                  |                                                   | 0.625                                             | 357                                  |
| 246             |                    |                         | +                  |                                                   | 1.059                                             | 64                                   |
| 247             |                    |                         | +                  |                                                   | 0.967                                             | 268                                  |
| 248             |                    |                         | +                  |                                                   | 0.747                                             | 32                                   |

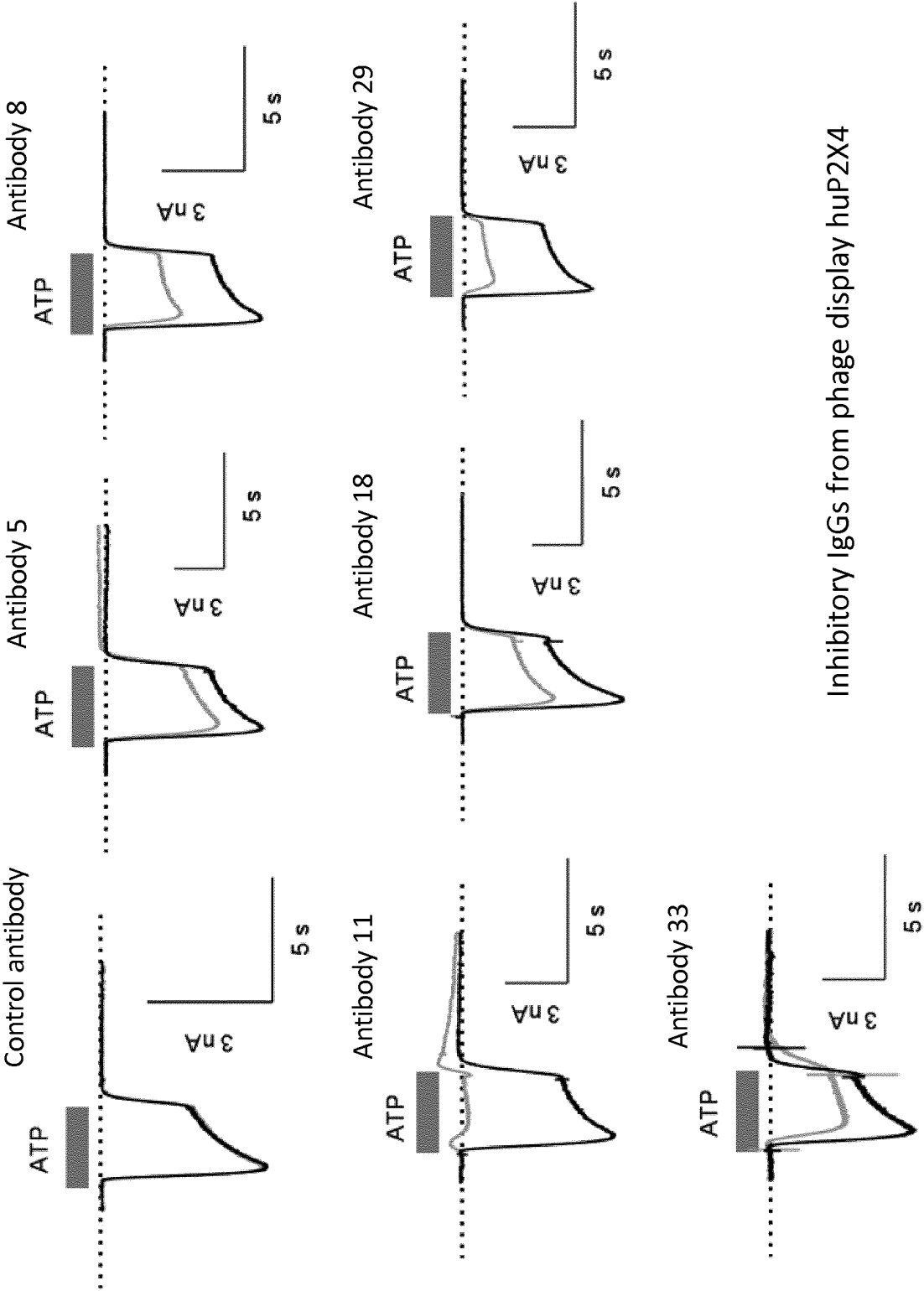
**Figure 7: Part 1i**

| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 249             |                    |                         | +                  |                                                   | 0.535                                             | 153                                  |
| 250             |                    |                         | +                  |                                                   | 0.800                                             | 53                                   |
| 251             |                    |                         | +                  |                                                   | 0.460                                             | 199                                  |
| 252             |                    |                         | +                  |                                                   | 1.979                                             | <LOD                                 |
| 253             |                    |                         | +                  |                                                   | 1.036                                             | 252                                  |
| 254             |                    |                         | +                  |                                                   | 1.097                                             | 144                                  |
| 255             |                    |                         | +                  |                                                   | 0.926                                             | 273                                  |
| 256             |                    |                         | +                  |                                                   | 0.688                                             | 392                                  |
| 257             |                    |                         | +                  |                                                   | 1.316                                             | <LOD                                 |
| 258             |                    |                         | +                  |                                                   | 0.606                                             | 67                                   |
| 259             |                    |                         | +                  |                                                   | 1.145                                             | 57                                   |
| 260             |                    |                         | +                  |                                                   | 0.585                                             | 244                                  |
| 261             |                    |                         | +                  |                                                   | 0.691                                             | 79                                   |
| 262             |                    |                         | +                  |                                                   | 0.557                                             | 220                                  |
| 263             |                    |                         | +                  |                                                   | 1.286                                             | 92                                   |
| 264             |                    |                         | +                  |                                                   | 0.161                                             | 66                                   |
| 265             |                    |                         | +                  |                                                   | 1.076                                             | <LOD                                 |
| 266             | -                  |                         | +                  |                                                   | 0.463                                             | 61                                   |
| 267             |                    |                         | +                  |                                                   | 0.443                                             | 49                                   |
| 268             |                    |                         | +                  |                                                   | 4.067                                             | 73                                   |
| 269             |                    |                         | +                  |                                                   | 0.757                                             | <LOD                                 |
| 270             |                    |                         | +                  |                                                   | 0.802                                             | 91                                   |
| 271             |                    |                         | +                  |                                                   | 0.696                                             | 112                                  |
| 272             |                    |                         | +                  |                                                   | 0.832                                             | 158                                  |
| 273             |                    |                         | +                  |                                                   | 0.814                                             | 403                                  |
| 274             |                    |                         | +                  |                                                   | 0.801                                             | 300                                  |
| 275             |                    |                         | +                  |                                                   | 0.982                                             | 141                                  |

**Figure 7: Part 1j**

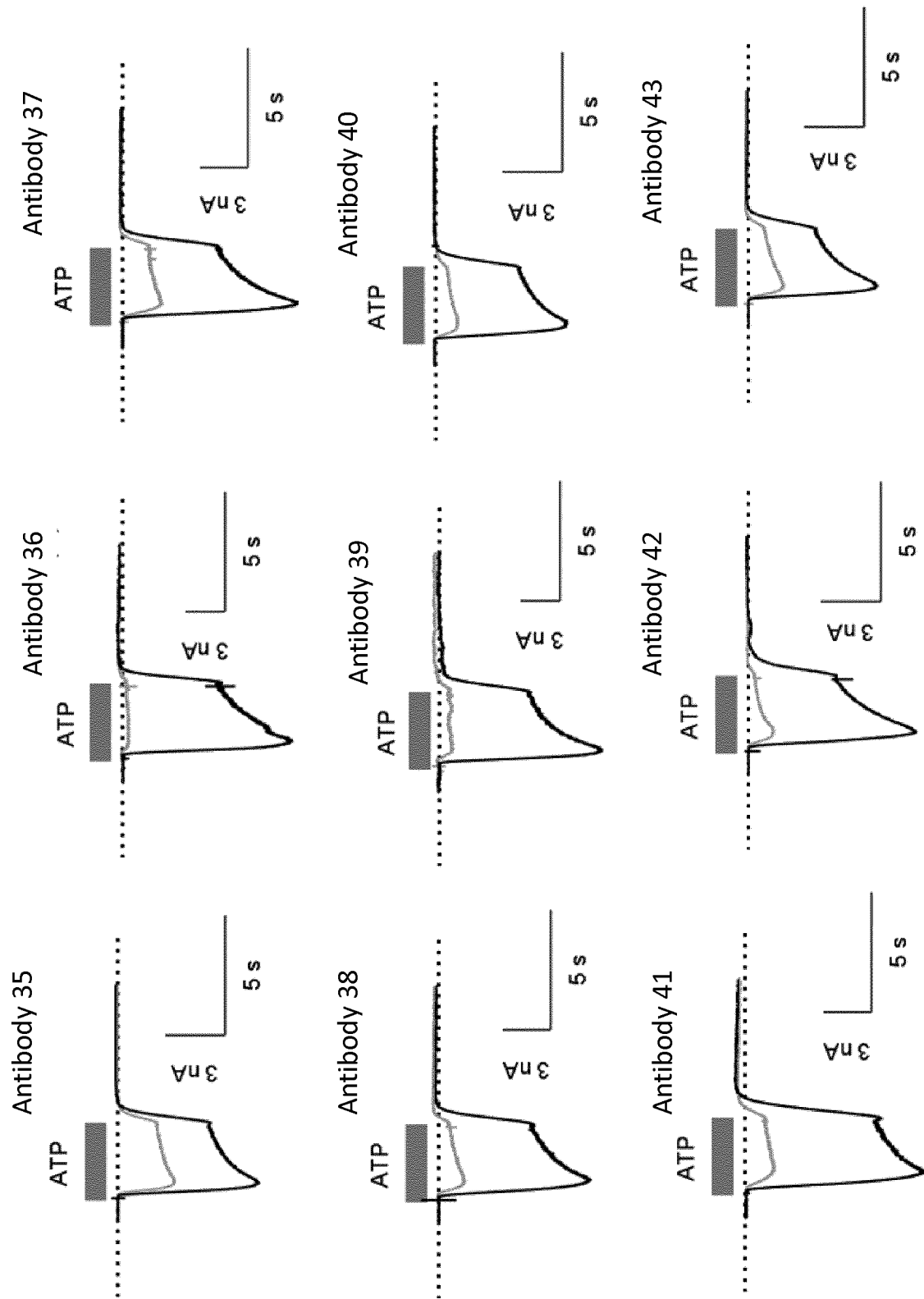
| Antibody number | Human P2X4 binding | Cynomolgus P2X4 binding | Mouse P2X4 binding | Fraction of control current at Human P2X4 (ephys) | Fraction of control current at Mouse P2X4 (ephys) | Concentration in ephys assay (mg/ml) |
|-----------------|--------------------|-------------------------|--------------------|---------------------------------------------------|---------------------------------------------------|--------------------------------------|
| 276             |                    |                         | +                  |                                                   | 1.172                                             | 90                                   |
| 277             |                    |                         | +                  |                                                   | 0.936                                             | 136                                  |
| 278             |                    |                         | +                  |                                                   | 1.142                                             | 101                                  |
| 279             |                    |                         | +                  |                                                   | 0.640                                             | 359                                  |
| 280             |                    |                         | +                  |                                                   | 1.134                                             | 91                                   |
| 281             | -                  | -                       | +                  | 0.800                                             | 0.098                                             | 306                                  |
| 282             |                    |                         | +                  |                                                   | 1.342                                             | 25                                   |
| 283             |                    |                         | +                  |                                                   | 0.730                                             | 78                                   |
| 284             |                    |                         | +                  |                                                   | 1.665                                             | 94                                   |
| 285             |                    |                         | +                  |                                                   | 0.436                                             | 55                                   |
| 286             |                    |                         | +                  |                                                   | 0.753                                             | <LOD                                 |

Figure 8A



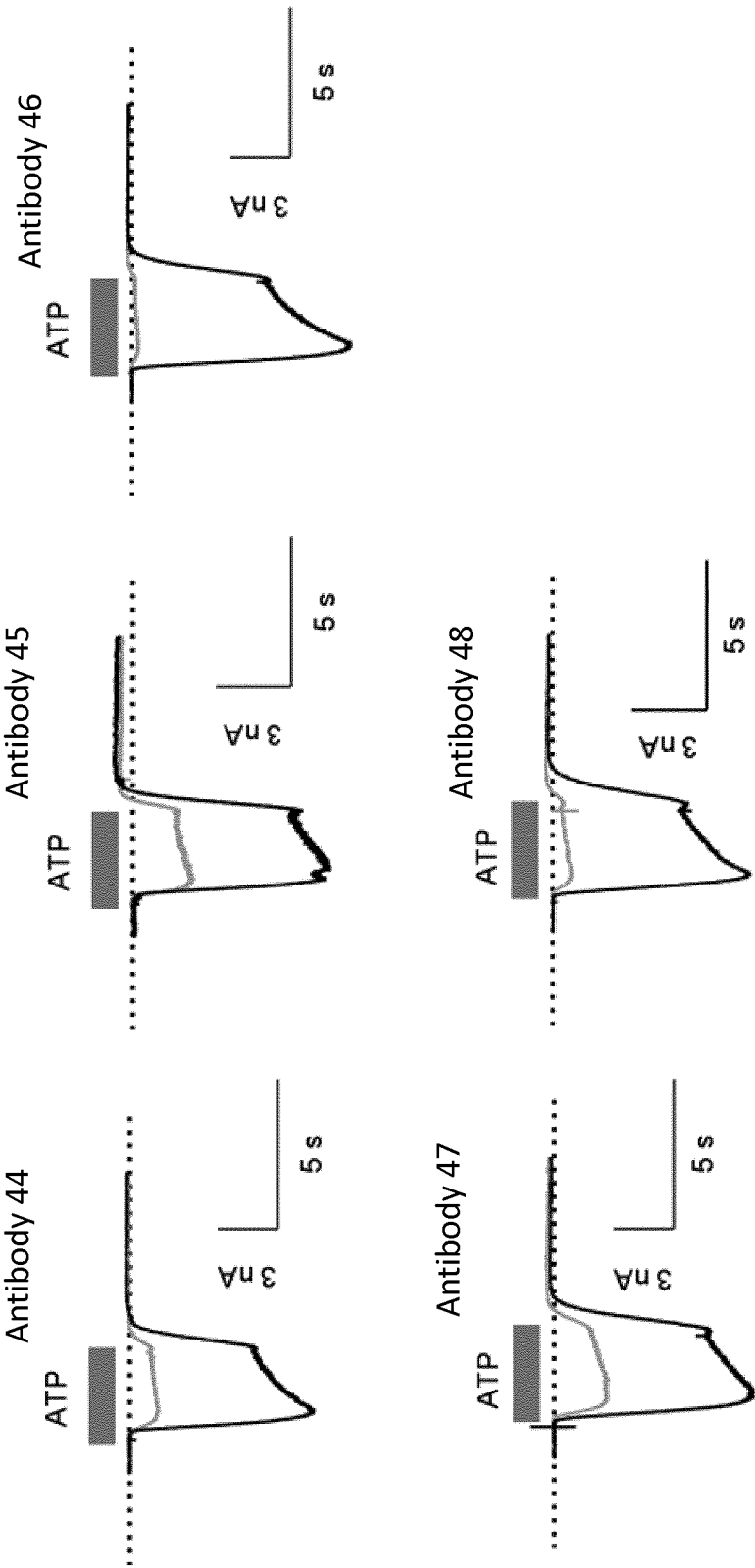
Inhibitory IgGs from phage display huP2X4

Figure 8B



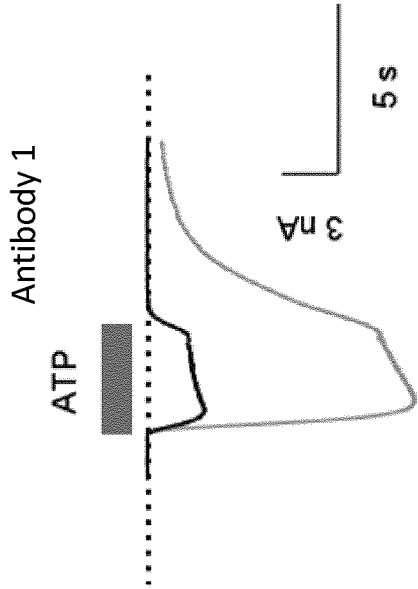
Inhibitory IgGs from hybridoma - activity against mP2X4

Figure 8C



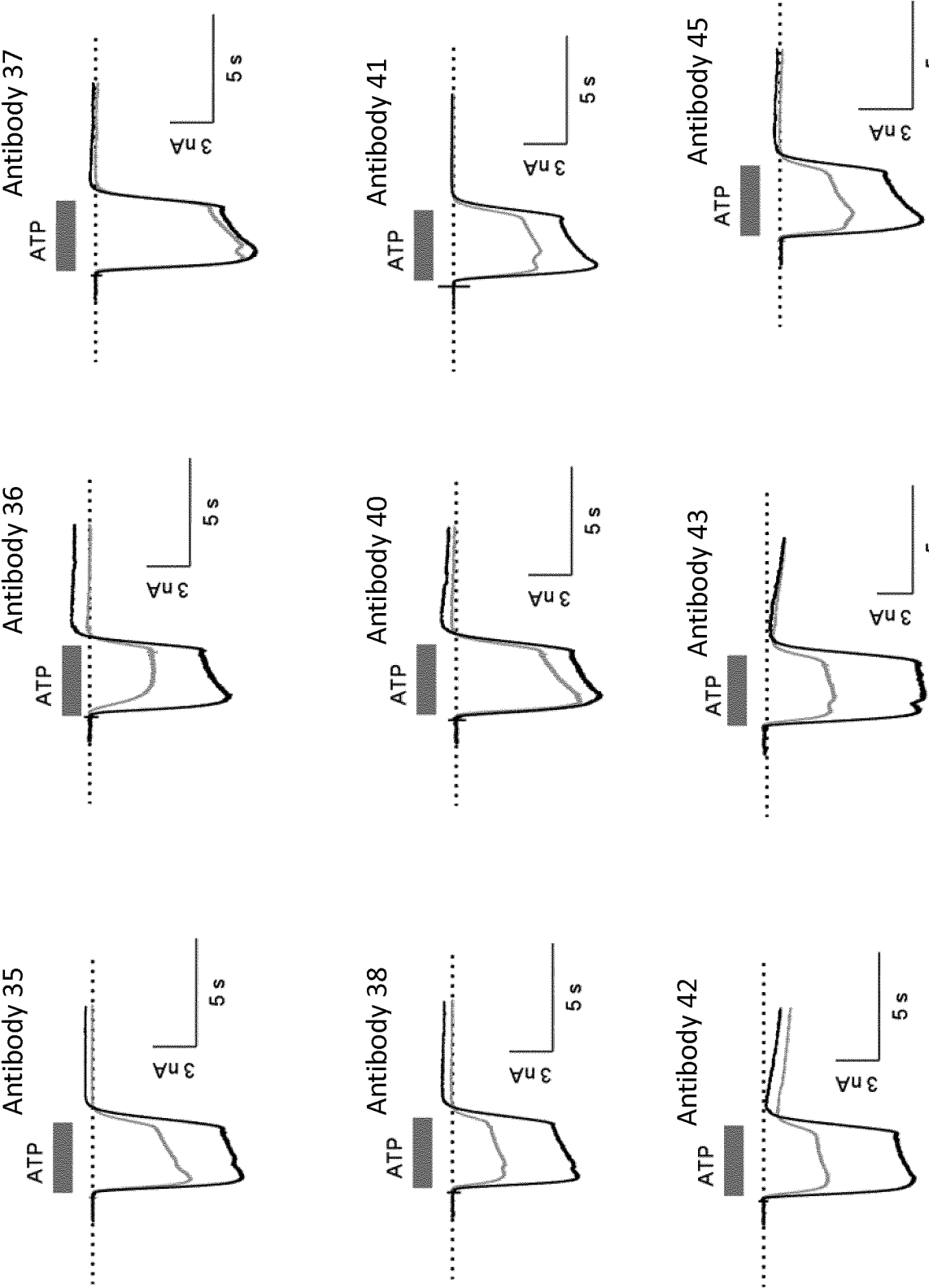
Inhibitory IgGs from hybridoma - activity against mP2X4

Figure 8D



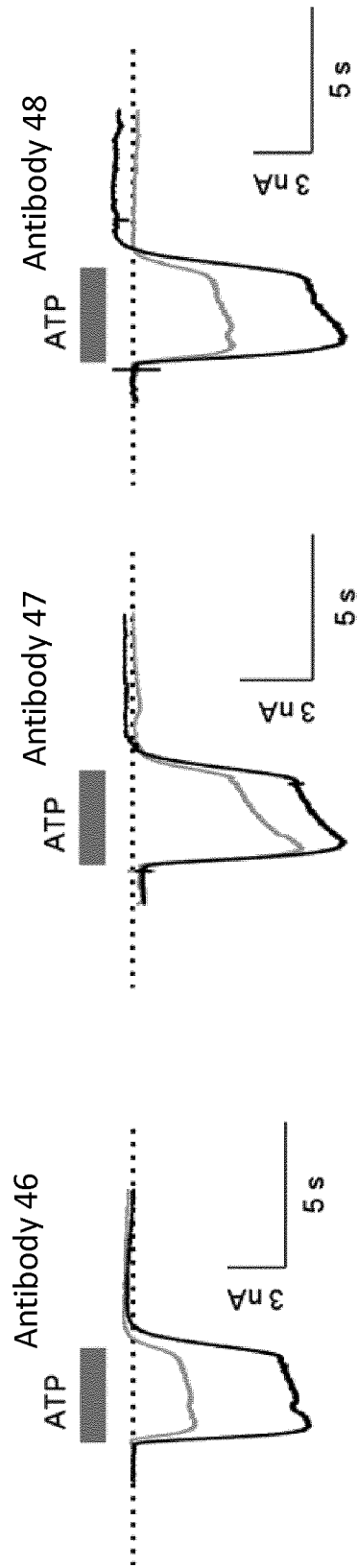
Example of a potentiating IgG - activity against huP2X4

Figure 8E



Inhibitory IgGs from hybridoma - activity against huP2X4

Figure 8F



Inhibitory IgGs from hybridoma - activity against huP2X4

Figure 9

Bipartite epitope-paratope interface – Antibody No. 11 VHCDRs-P2X4 protomer 1 head (major interface); Antibody No. 11 VLCDRs-P2X4 protomer 2 right flipper (minor interface).

Three Antibody No. 11 molecules can potentially bind the same P2X4 trimer molecule.  
The two Fab arms of Antibody No. 11 are not likely to engage the same P2X4 trimer molecule.  
The ab is predicted to bind a P2X heteromer across the epitope formed by two P2X4 subunits.

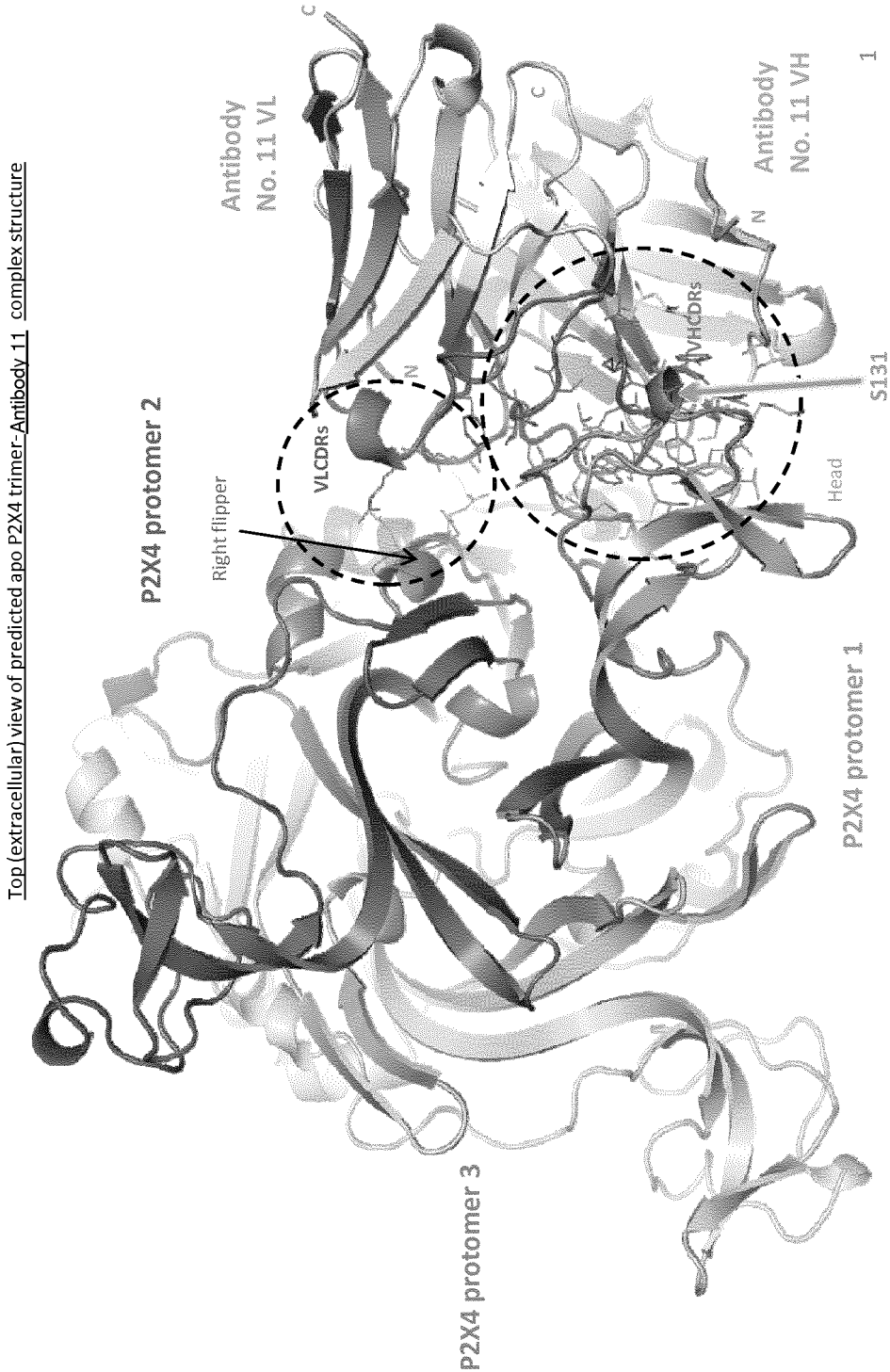
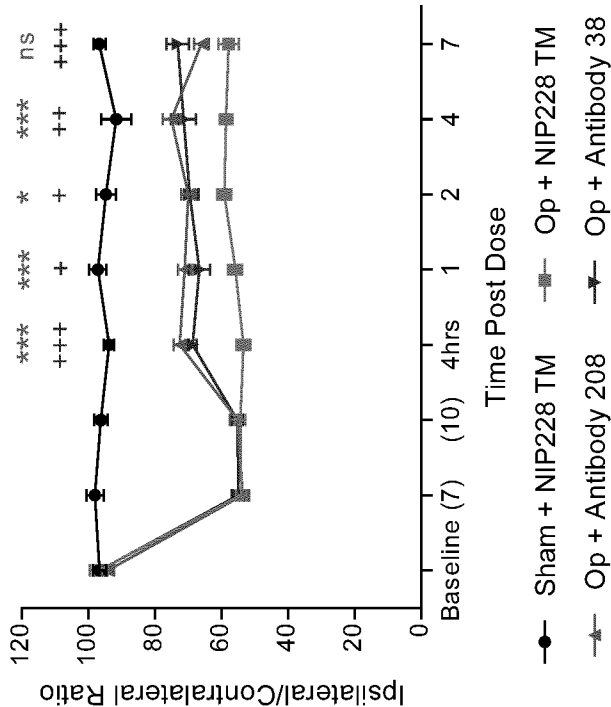




Figure 11



[illegible]

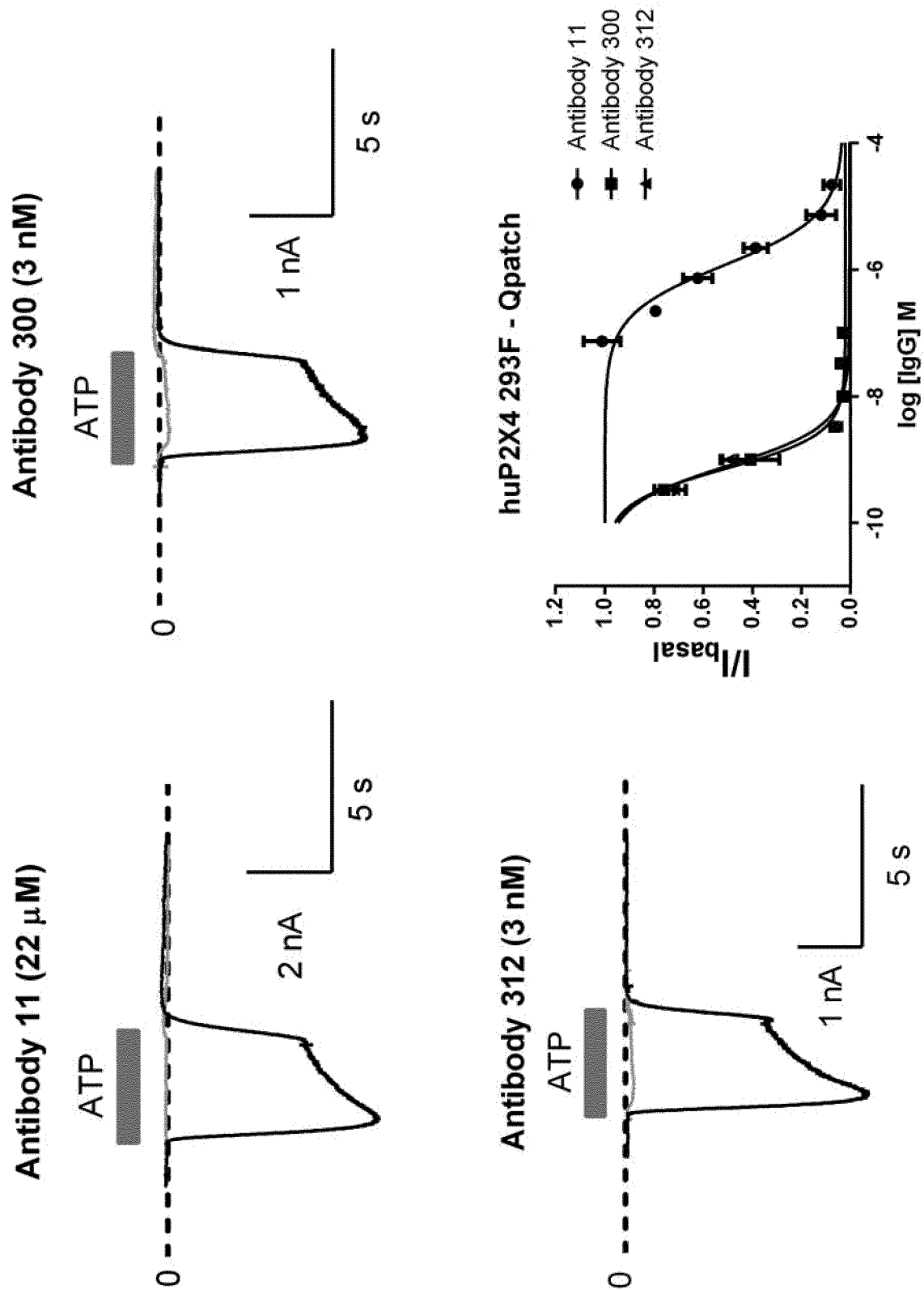
[illegible]

[illegible]

[illegible]



Figure 14: Activity of antibodies in a huP2X4 electrophysiology assay



**Figure 15: Potency of Antibody 11 optimized antibodies at huP2X4**

| Antibody number | Geometric mean IC <sub>50</sub> (Molar) huP2X4 FLIPR assay | IC <sub>50</sub> (Molar) huP2X4 Ephys (HEK293f) |
|-----------------|------------------------------------------------------------|-------------------------------------------------|
| 287             | 3.9E-08                                                    | 3.5E-09                                         |
| 288             |                                                            | 4.7E-08                                         |
| 289             |                                                            | 4.5E-08                                         |
| 290             | 4.6E-07                                                    | 2.6E-09                                         |
| 291             | 1.1E-07                                                    | 4.9E-09                                         |
| 292             | 1.8E-07                                                    | 7.4E-09                                         |
| 293             | 7.7E-08                                                    | 4.9E-09                                         |
| 294             | 1.6E-07                                                    | 1.5E-08                                         |
| 295             | 2.4E-07                                                    | 1.2E-09                                         |
| 296             | 4.5E-08                                                    | 1.3E-09                                         |
| 297             | 5.3E-08                                                    | 1.8E-09                                         |
| 298             | 2.9E-08                                                    | 1.1E-09                                         |
| 299             |                                                            | 2.2E-09                                         |
| 300             | 7.9E-09                                                    | 7.1E-10                                         |
| 302             | 8.0E-10                                                    | 5.6E-10                                         |
| 303             | 1.9E-07                                                    | 2.4E-09                                         |
| 304             | 9.5E-08                                                    | 2.4E-09                                         |
| 305             |                                                            | >1E-07                                          |
| 306             |                                                            | >1E-07                                          |
| 307             |                                                            | >1E-07                                          |
| 308             | 7.0E-10                                                    | 6.1E-10                                         |
| 309             | 7.3E-08                                                    | 1.2E-09                                         |
| 310             |                                                            | 6.2E-09                                         |
| 311             | 4.0E-10                                                    | 5.0E-10                                         |
| 312             | 5.8E-10                                                    | 5.3E-10                                         |
| 313             | 3.3E-10                                                    | 5.4E-10                                         |
| 314             | 3.5E-08                                                    | 1.1E-09                                         |
| 315             | 3.0E-10                                                    | 6.9E-10                                         |

blank = data not disclosed

**Figure 16: Potency of hybridoma derived antibodies at mouse and human P2X4**

| Antibody Number | IC <sub>50</sub> (Molar) huP2X4<br>Ephys (HEK293f) | n | IC <sub>50</sub> (Molar) moP2X4<br>Ephys (HEK293f) | n  |
|-----------------|----------------------------------------------------|---|----------------------------------------------------|----|
| 38              | 3.26E-07                                           | 3 | 4.89E-09                                           | 4  |
| 43              | NT                                                 |   | 8.13E-09                                           | 4  |
| 46              | 1.79E-07                                           | 4 | 2.03E-08                                           | 8  |
| 208             | > 30E-06                                           | 4 | 2.57E-08                                           | 16 |

NT indicates not tested

Figure 17: Effect of P2X4 antibodies on mouse microglial P2X4 currents

| Antibody Number | hulG1                 |              |    |                                     |  | rat IgG1              |              |    |                                     |
|-----------------|-----------------------|--------------|----|-------------------------------------|--|-----------------------|--------------|----|-------------------------------------|
|                 | Concentration (mg/ml) | Current (pA) | n  | Significant difference from Control |  | Concentration (mg/ml) | Current (pA) | n  | Significant difference from Control |
| Control IgG     | 0.33                  | -446.2       | 11 | -                                   |  | 0.4                   | -622.5       | 10 | -                                   |
| 38              | 0.33                  | -99.29       | 4  | N                                   |  | 0.11                  | -244.6       | 5  | N                                   |
| 43              | 0.33                  | -332.3       | 3  | N                                   |  | -                     | NT           | -  | -                                   |
| 46              | 0.33                  | 9.06         | 3  | Y                                   |  | 0.25                  | 40.96        | 7  | Y                                   |
| 208             | 0.33                  | 12.12        | 4  | Y                                   |  | 0.4                   | 35.09        | 3  | Y                                   |

Figure 18: Exemplar effect of antibody 208 on native P2X4 currents in primary mouse microglia

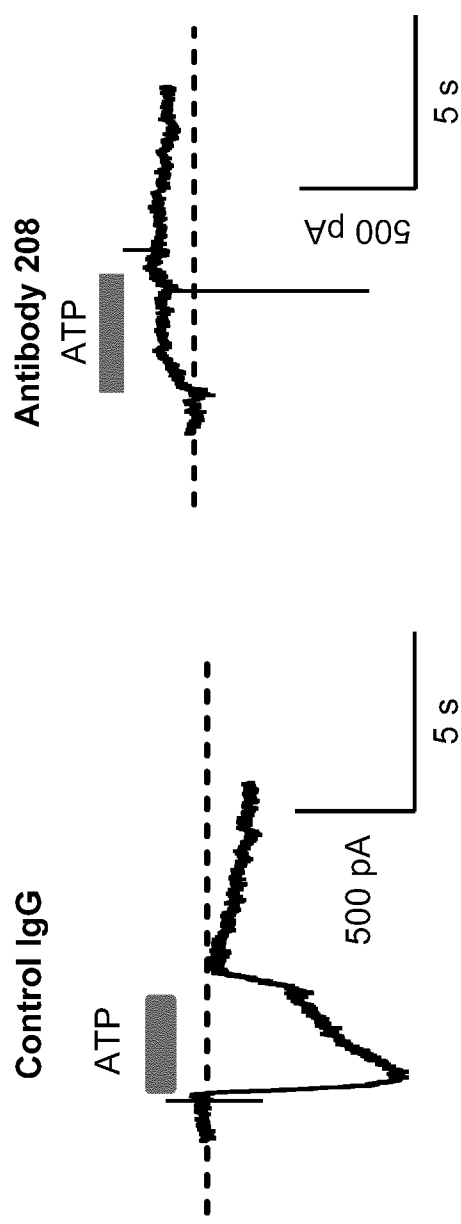


Figure 19. Example of activity of two anti-P2X4 antibodies in a calcium flux assay.

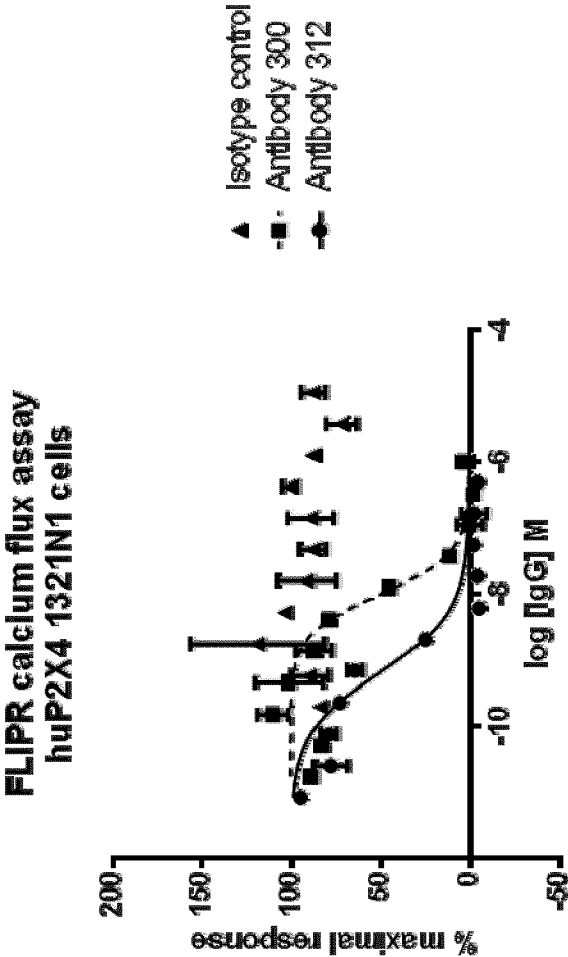
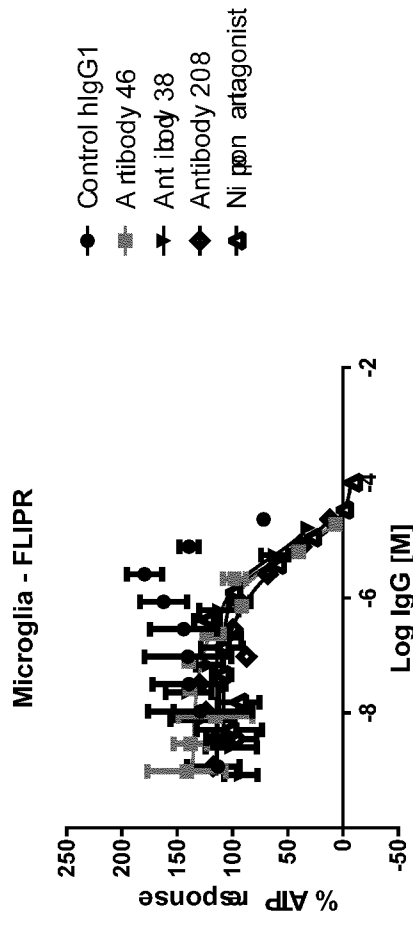


Figure 20: Effect of mouse reactive P2X4 antibodies on native mouse microglial P2X4 assayed on FLIPR



| Antibody Number   | IC <sub>50</sub> moP2X4 FLIPR (microglia) | n |
|-------------------|-------------------------------------------|---|
| 38                | 5.0E-06                                   | 2 |
| 46                | 1.6E-05                                   | 2 |
| 208               | 9.3E-06                                   | 2 |
| Nippon antagonist | 5.6E-06                                   | 2 |

Figure 21: Exemplary electrophysiology current traces from human monocyte derived macrophages

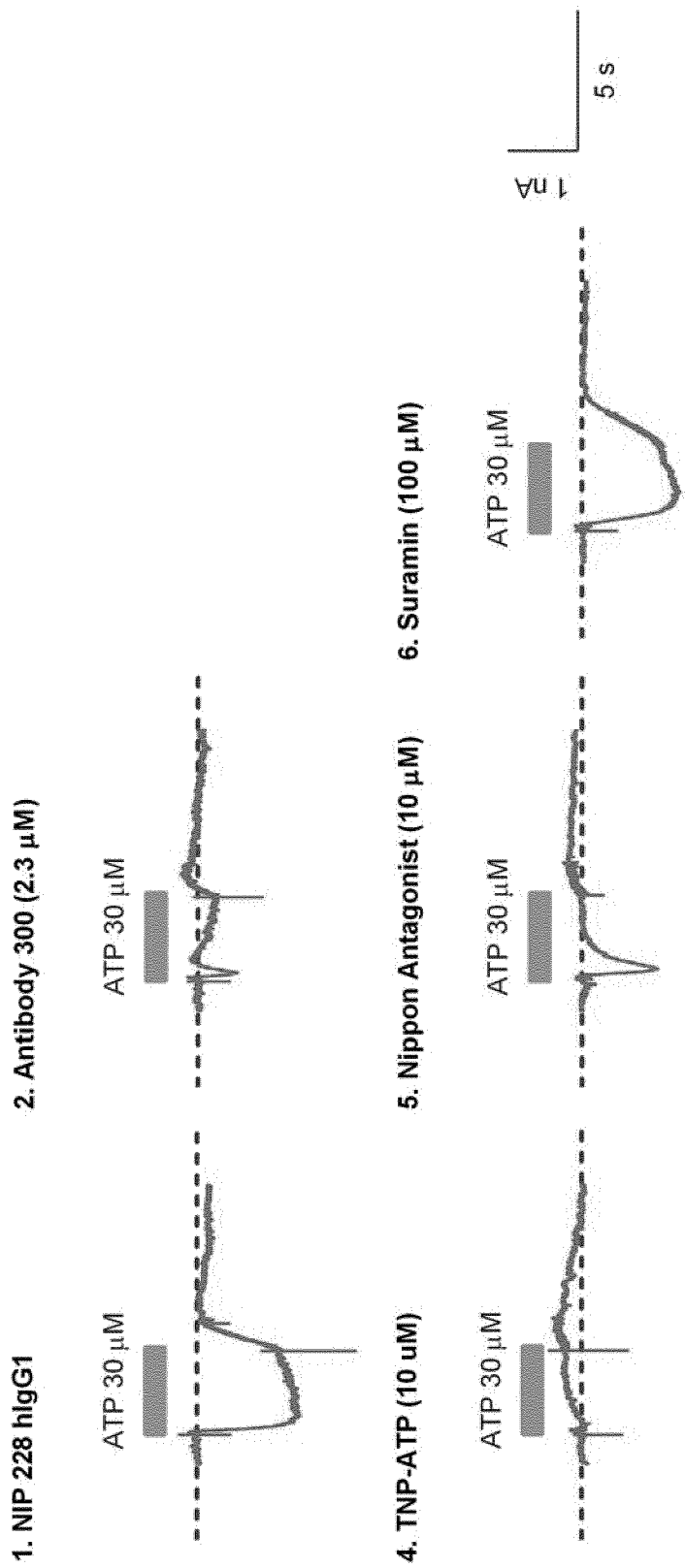


Figure 22: Summary of the effect of P2X4 antibodies on human monocyte derived macrophage, ATP induced currents.

| Nickname          | Antibody number | Donor 1          |         |   | Donor 2          |         |   |
|-------------------|-----------------|------------------|---------|---|------------------|---------|---|
|                   |                 | Mean Current (A) | SD      | n | Mean Current (A) | SD      | n |
| NIP 228           |                 | -1.4E-09         | 1.3E-09 | 8 | -7.0E-10         | 1.3E-09 | 7 |
|                   | 300             | -2.5E-11         | 2.4E-10 | 5 | 1.4E-12          | 3.2E-10 | 7 |
| TNP ATP           |                 | 3.6E-10          | 3.1E-10 | 7 |                  |         |   |
| Nippon Antagonist |                 |                  |         |   | 1.3E-10          | 7.4E-11 | 6 |

<110> Williams, Wendy  
 Jones, Clare  
 Button, James  
 Linley, John  
 Snijder, Arjan  
 Huang, Ling  
 Shibata, Yoko  
 Sridharan, Sudharsan  
 Dobson, Claire  
 Groves, Maria

<120> Ion Channel Modulators and Uses thereof

<140>

<141> 01-May-2015

<150> 61/987,929

<151> 02-May-2014

<160> 378

<170> Medimmune Ltd patent software March 2010 release. Output verified by  
 USPTO Checker version 4.4.0.

<210> 1

<211> 387

<212> DNA

<213> Homo sapiens

<400> 1

```

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc      60
tcctgtgcag cctctggatt cacctttagc ggctatgcca tgagctgggt ccgccaggct      120
ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac      180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cagctgtat      240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagaagaa      300
cgaggagatt actttggttt tagtggttat tactacacat actactttga ctactggggc      360
cgagggacaa tggtcaccgt ctcgagt      387

```

<210> 2

<211> 129

<212> PRT

<213> Homo sapiens

<400> 2

```

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                    5          10          15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Gly Tyr
                20          25          30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                35          40          45
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
                50          55          60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
        65          70          75          80

```

eolf-seql.txt

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Glu Glu Arg Gly Ser Tyr Phe Gly Phe Ser Gly Tyr Tyr Tyr  
100 105 110

Thr Tyr Tyr Phe Asp Tyr Trp Gly Arg Gly Thr Met Val Thr Val Ser  
115 120 125

Ser

<210> 3  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 3  
Gly Tyr Ala Met Ser  
5

<210> 4  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 4  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 5  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 5  
Glu Glu Arg Gly Ser Tyr Phe Gly Phe Ser Gly Tyr Tyr Tyr Thr Tyr  
5 10 15

Tyr Phe Asp Tyr  
20

<210> 6  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 6  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 7  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 7

eolf-seql.txt

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 8  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 8  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 9  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 9  
Trp Gly Arg Gly Thr Met Val Thr Val Ser Ser  
5 10

<210> 10  
<211> 327  
<212> DNA  
<213> Homo sapiens

<400> 10  
caggctgtgc tgactcagcc gtcctcagtg tctggggccc cagggcagag ggtcaccatc 60  
tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtacactg gtaccagcag 120  
cttccaggaa cagcccccaa actcctcatc tacggtaaca acaatcggcc ctccggggctc 180  
cctgaccgat tctctggctc caagtctggc acctcagcct ccctggccat cactgggctc 240  
caggctgagg atgaagctga ttattactgc cagtcctatg acaccaacct gaaagttttt 300  
ggcggaggga ccaagctgac cgtccta 327

<210> 11  
<211> 109  
<212> PRT  
<213> Homo sapiens

<400> 11  
Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ala Pro Gly Gln  
5 10 15  
Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly  
20 25 30  
Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu  
35 40 45  
Leu Ile Tyr Gly Asn Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe  
50 55 60  
Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu  
65 70 75 80  
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Thr Asn

85

90

95

Leu Lys Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
 100 105

<210> 12  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 12  
 Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His  
 5 10

<210> 13  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 13  
 Gly Asn Asn Asn Arg Pro Ser  
 5

<210> 14  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 14  
 Gln Ser Tyr Asp Thr Asn Leu Lys Val  
 5

<210> 15  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 15  
 Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ala Pro Gly Gln  
 5 10 15

Arg Val Thr Ile Ser Cys  
 20

<210> 16  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 16  
 Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr  
 5 10 15

<210> 17  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 17  
 Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser  
 5 10 15

eolf-seql.txt

Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
 20 25 30

<210> 18  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 18  
 Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
 5 10

<210> 19  
 <211> 363  
 <212> DNA  
 <213> Homo sapiens

<400> 19  
 cagggtgcagc tgggtgcaatc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60  
 tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120  
 cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180  
 agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240  
 ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagccggact 300  
 ggggattact actactacgg tatggacgtc tggggcaaag ggacaatggt caccgtctcg 360  
 agt 363

<210> 20  
 <211> 121  
 <212> PRT  
 <213> Homo sapiens

<400> 20  
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu  
 5 10 15  
 Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr  
 20 25 30  
 Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met  
 35 40 45  
 Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe  
 50 55 60  
 Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr  
 65 70 75 80  
 Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys  
 85 90 95  
 Ala Ser Arg Thr Gly Asp Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly  
 100 105 110  
 Lys Gly Thr Met Val Thr Val Ser Ser  
 115 120

<210> 21  
 <211> 5

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 21  
Ser Tyr Trp Ile Gly  
5

<210> 22  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 22  
Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln  
5 10 15

Gly

<210> 23  
<211> 12  
<212> PRT  
<213> Homo sapiens

<400> 23  
Arg Thr Gly Asp Tyr Tyr Tyr Tyr Gly Met Asp Val  
5 10

<210> 24  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 24  
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu  
5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr  
20 25 30

<210> 25  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 25  
Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly  
5 10

<210> 26  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 26  
Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln  
5 10 15

Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Ser  
20 25 30

<210> 27

eolf-seql.txt

<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 27  
Trp Gly Lys Gly Thr Met Val Thr Val Ser Ser  
5 10

<210> 28  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 28  
tcctatgtgc tgactcagcc accctcggtg tcagtgtccc taggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaagcaa tatgcttatt ggtaccagca gaagccaggc 120  
caggcccctg tgctggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccagctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacttatgt ggtattcggc 300  
ggagggacca agctgaccgt ccta 324

<210> 29  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 29  
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Leu Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Lys Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Ser Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
100 105

<210> 30  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 30  
Ser Gly Asp Ala Leu Pro Lys Gln Tyr Ala Tyr  
5 10

<210> 31  
<211> 7

<212> PRT  
 <213> Homo sapiens

<400> 31  
 Lys Asp Ser Glu Arg Pro Ser  
 5

<210> 32  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 32  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
 5 10

<210> 33  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 33  
 Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Leu Gly Gln  
 5 10 15  
 Thr Ala Arg Ile Thr Cys  
 20

<210> 34  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 34  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
 5 10 15

<210> 35  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 35  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Ser Ser Gly Thr Thr Val Thr  
 5 10 15  
 Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
 20 25 30

<210> 36  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 36  
 Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
 5 10

<210> 37  
 <211> 378  
 <212> DNA  
 <213> Homo sapiens

eolf-seql.txt

```
<400>    37
gaggtgcagc tgggtgcagtc tgggggaggc ctggtacagc ctggcaggtc cctgagactc      60
tcctgtacag cctctggatt cacctttgat gattattcca tgcactgggt cgggcaagct      120
ccaggggaagg gcctggagtg ggtctcaagt attagttgga gtagtggtag cataggctat      180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccttgtct      240
ctgcaaatga acagtctgag agttgaggac acggccttgt attactgtgt aaaggatcga      300
atgtattact atgatactgg tggatattat tctggttttg atatgtgggg ccaagggaca      360
atggtcaccg tctcgagt                                     378
```

```
<210>    38
<211>   126
<212>    PRT
<213>   Homo sapiens
```

```
<400>    38
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
              5              10              15
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp Asp Tyr
              20              25              30
Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
              35              40              45
Ser Ser Ile Ser Trp Ser Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
              50              55              60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Ser
              65              70              75              80
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
              85              90              95
Val Lys Asp Arg Met Tyr Tyr Tyr Asp Thr Gly Gly Tyr Tyr Ser Gly
              100              105              110
Phe Asp Met Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
              115              120              125
```

```
<210>    39
<211>     5
<212>    PRT
<213>   Homo sapiens
```

```
<400>    39
Asp Tyr Ser Met His
              5
```

```
<210>    40
<211>    17
<212>    PRT
<213>   Homo sapiens
```

```
<400>    40
Ser Ile Ser Trp Ser Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val Lys
              5              10              15
```

Gly

eolf-seql.txt

<210> 41  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 41  
 Asp Arg Met Tyr Tyr Tyr Asp Thr Gly Gly Tyr Tyr Ser Gly Phe Asp  
                   5                  10                  15

Met

<210> 42  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 42  
 Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Arg  
                   5                  10                  15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp  
                   20                  25                  30

<210> 43  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 43  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 44  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 44  
 Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Ser Leu Gln  
                   5                  10                  15

Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys Val Lys  
                   20                  25                  30

<210> 45  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 45  
 Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser  
                   5                  10

<210> 46  
 <211> 318  
 <212> DNA  
 <213> Homo sapiens

<400> 46

eolf-seql.txt

```
tcctatgagc tgactcagcc accctcagtg tccgtgtccc caggacagac agccaccatc      60
acctgctctg gagataaatt ggatgataaa tatatatctt ggtatcaaag gaagccaggc      120
cagtcacctg tcctgctcat ctatcaagat atagagcggc cctcagggat ccctgaccga      180
ttctctggct ctaattctgg gaacacagcc actctgtcca tcagcggggac ccagtctatg      240
gatgaggctg agtattactg tcaggcgtgg gacaacggtg ctattgtatt cggcggaggg      300
accaagctga ccgtccta                                     318
```

<210> 47  
 <211> 106  
 <212> PRT  
 <213> Homo sapiens

<400> 47  
 Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Thr Ile Thr Cys Ser Gly Asp Lys Leu Asp Asp Lys Tyr Ile  
                   20                  25                  30  
 Ser Trp Tyr Gln Arg Lys Pro Gly Gln Ser Pro Val Leu Leu Ile Tyr  
                   35                  40                  45  
 Gln Asp Ile Glu Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Asn Ser Gly Asn Thr Ala Thr Leu Ser Ile Ser Gly Thr Gln Ser Met  
 65                  70                  75                  80  
 Asp Glu Ala Glu Tyr Tyr Cys Gln Ala Trp Asp Ser Gly Ala Ile Val  
                   85                  90                  95  
 Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
                   100                  105

<210> 48  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 48  
 Ser Gly Asp Lys Leu Asp Asp Lys Tyr Ile Ser  
                   5                  10

<210> 49  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 49  
 Gln Asp Ile Glu Arg Pro Ser  
                   5

<210> 50  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 50  
 Gln Ala Trp Asp Ser Gly Ala Ile Val

5

<210> 51  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 51  
 Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Thr Ile Thr Cys  
                   20

<210> 52  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 52  
 Trp Tyr Gln Arg Lys Pro Gly Gln Ser Pro Val Leu Leu Ile Tyr  
                   5                  10                  15

<210> 53  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 53  
 Gly Ile Pro Asp Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr  
                   5                  10                  15  
 Leu Ser Ile Ser Gly Thr Gln Ser Met Asp Glu Ala Glu Tyr Tyr Cys  
                   20                  25                  30

<210> 54  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 54  
 Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
                   5                  10

<210> 55  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 55  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120  
 ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
 gatttttggg gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

eolf-seql.txt

<210> 56  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 56  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
                   50                  55                  60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
  65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
                   100                  105                  110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   115                  120                  125

<210> 57  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 57  
 Ser Tyr Ala Met Ser  
                   5

<210> 58  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 58  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
                   5                  10                  15

Gly

<210> 59  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 59  
 Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 60  
 <211> 30

eolf-seql.txt

<212> PRT  
 <213> Homo sapiens  
 <400> 60  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 61  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens  
 <400> 61  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 62  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens  
 <400> 62  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 63  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens  
 <400> 63  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 64  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens  
 <400> 64  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggcccctc tactgggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 65  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 65  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
 65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 66  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 66  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 67  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 67  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 68  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 68  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                   5                  10

<210> 69  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 69  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys  
                   20

<210> 70  
 <211> 15

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 70  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 71  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 71  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 72  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 72  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 73  
<211> 363  
<212> DNA  
<213> Homo sapiens

<400> 73  
gaggtgcagc tgggtggagtc cgggggaggc ttggtccagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt tacctttagt aggtattgga tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtggccaac ataaaggaag atggaagtga gaaaaactat 180  
gtggactctg tgaagggccg actcaccatc tccagagaca acgccaagaa ctactgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgtgc gaactactat 300  
gatagtagtg gttattatgc ccttgatagc tggggccgag gcaccctggt cactgtctcc 360  
tca 363

<210> 74  
<211> 121  
<212> PRT  
<213> Homo sapiens

<400> 74  
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr  
20 25 30  
Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ala Asn Ile Lys Glu Asp Gly Ser Glu Lys Asn Tyr Val Asp Ser Val

eolf-seql.txt

50

55

60

Lys Gly Arg Leu Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Asn Tyr Tyr Asp Ser Ser Gly Tyr Tyr Ala Leu Asp Ser Trp Gly  
100 105 110  
Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120

<210> 75  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 75  
Arg Tyr Trp Met Ser  
5

<210> 76  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 76  
Asn Ile Lys Glu Asp Gly Ser Glu Lys Asn Tyr Val Asp Ser Val Lys  
5 10 15

Gly

<210> 77  
<211> 12  
<212> PRT  
<213> Homo sapiens

<400> 77  
Tyr Tyr Asp Ser Ser Gly Tyr Tyr Ala Leu Asp Ser  
5 10

<210> 78  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 78  
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 79  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 79  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala

5

10

<210> 80  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 80  
 Arg Leu Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Asn  
                   20                  25                  30

<210> 81  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 81  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 82  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 82  
 tcctatgagc tgactcagcc accctcagt tccgtgtccc caggacagac agccaccatc 60  
 acctgctctg gagatgcatt gacaaaacaa tatgcttttt ggtaccaaca gaagccaggc 120  
 caggccccta tattggatgat ctttagagac tctgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccagctcagg gacaacagcg acgttgacca tcagtggggg ccaggcagga 240  
 gacgaggctg actattactg tcaatctaca gacaatactg cgacctccgt cgtcttcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 83  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 83  
 Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Thr Ile Thr Cys Ser Gly Asp Ala Leu Thr Lys Gln Tyr Ala  
                   20                  25                  30  
 Phe Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Ile Leu Val Ile Phe  
                   35                  40                  45  
 Arg Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Ser Ser Gly Thr Thr Ala Thr Leu Thr Ile Ser Gly Val Gln Ala Gly  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Thr Asp Asn Thr Ala Thr Ser  
                   85                  90                  95

eolf-seql.txt

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 84  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 84  
Ser Gly Asp Ala Leu Thr Lys Gln Tyr Ala Phe  
5 10

<210> 85  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 85  
Arg Asp Ser Glu Arg Pro Ser  
5

<210> 86  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 86  
Gln Ser Thr Asp Asn Thr Ala Thr Ser Val Val  
5 10

<210> 87  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 87  
Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Thr Ile Thr Cys  
20

<210> 88  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 88  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Ile Leu Val Ile Phe  
5 10 15

<210> 89  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 89  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Ser Ser Gly Thr Thr Ala Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Gly Asp Glu Ala Asp Tyr Tyr Cys  
Page 19

<210> 90  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 90  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 91  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 91  
 gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt ccgccaggct 120  
 ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagacccgag 300  
 ctccctgaga cagctatggt tagaaactgg cacttcgatc tctggggcca ggggacaatg 360  
 gtcaccgtct cgagt 375

<210> 92  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 92  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
                   50                  55                  60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
                   65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Ala Arg Pro Glu Leu Pro Glu Thr Ala Met Val Arg Asn Trp His Phe  
                   100                  105                  110  
 Asp Leu Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser  
                   115                  120                  125

<210> 93  
 <211> 5  
 <212> PRT

<213> Homo sapiens

<400> 93  
Ser Tyr Ala Met Ser  
5

<210> 94  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 94  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 95  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 95  
Pro Glu Leu Pro Glu Thr Ala Met Val Arg Asn Trp His Phe Asp Leu  
5 10 15

<210> 96  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 96  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 97  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 97  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 98  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 98  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 99  
<211> 11

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 99  
Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser  
5 10

<210> 100  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 100  
tcctatgtgc tgactcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaagcaa tatgcttatt ggtaccagca gaagccaggc 120  
caggcccctg tgctggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccagctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gatgaggctg actattactg tcaatcagca gacagcagtg gtacttatgt ggtattcggc 300  
ggagggacca agctgaccgt ccta 324

<210> 101  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 101  
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Lys Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Ser Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
100 105

<210> 102  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 102  
Ser Gly Asp Ala Leu Pro Lys Gln Tyr Ala Tyr  
5 10

<210> 103  
<211> 7  
<212> PRT

```

<213> Homo sapiens

<400> 103
Lys Asp Ser Glu Arg Pro Ser
5

<210> 104
<211> 11
<212> PRT
<213> Homo sapiens

<400> 104
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val
5 10

<210> 105
<211> 22
<212> PRT
<213> Homo sapiens

<400> 105
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
5 10 15

Thr Ala Arg Ile Thr Cys
20

<210> 106
<211> 15
<212> PRT
<213> Homo sapiens

<400> 106
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
5 10 15

<210> 107
<211> 32
<212> PRT
<213> Homo sapiens

<400> 107
Gly Ile Pro Glu Arg Phe Ser Gly Ser Ser Ser Gly Thr Thr Val Thr
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys
20 25 30

<210> 108
<211> 10
<212> PRT
<213> Homo sapiens

<400> 108
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
5 10

<210> 109
<211> 387
<212> DNA
<213> Homo sapiens

```

eolf-seql.txt

```
<400> 109
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60
tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt cgcagggt 120
ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cagctgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagaagcttt 300
cattattgta gtagtaccaa ctgctatgtg gagggtcggg aaaactttga ctactggggc 360
caagggacaa tggtcaccgt ctcgagt 387
```

```
<210> 110
<211> 129
<212> PRT
<213> Homo sapiens
```

```
<400> 110
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Phe His Tyr Cys Ser Ser Thr Asn Cys Tyr Val Glu Gly
100 105 110
Arg Glu Asn Phe Asp Tyr Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125
Ser
```

```
<210> 111
<211> 5
<212> PRT
<213> Homo sapiens
```

```
<400> 111
Ser Tyr Ala Met Ser
5
```

```
<210> 112
<211> 17
<212> PRT
<213> Homo sapiens
```

```
<400> 112
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
5 10 15
```

Gly

<210> 113  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 113  
 Ser Phe His Tyr Cys Ser Ser Thr Asn Cys Tyr Val Glu Gly Arg Glu  
                   5                  10                  15  
 Asn Phe Asp Tyr  
                   20

<210> 114  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 114  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 115  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 115  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 116  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 116  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 117  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 117  
 Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser  
                   5                  10

<210> 118  
 <211> 318  
 <212> DNA  
 <213> Homo sapiens

eolf-seql.txt

```
<400> 118
tcctatgagc tgactcagcc accctcagtg tccgtgtccc cccgacagac agccagcatc 60
acctgctctg gagataaatt ggggaataaa tatgttctgt ggtatcaaca gaagccaggc 120
cactccccctg tactgggtcat ctatcaagat tccaagcggc cctcagggat ccctgagcga 180
ttctctgggt ccaactctgg gaacacagcc actctgacca tcagcgggac ccaggctatg 240
gatgaggctg tctattactg tcaggcgtgg gacagcacca tcgtggtctt cggcggaggg 300
accaagctga ccgtccta 318
```

```
<210> 119
<211> 106
<212> PRT
<213> Homo sapiens
```

```
<400> 119
Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Arg Gln
5 10 15
Thr Ala Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Asn Lys Tyr Ala
20 25 30
Ser Trp Tyr Gln Gln Lys Pro Gly His Ser Pro Val Leu Val Ile Tyr
35 40 45
Gln Asp Ser Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60
Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65 70 75 80
Asp Glu Ala Val Tyr Tyr Cys Gln Ala Trp Asp Ser Thr Ile Val Val
85 90 95
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105
```

```
<210> 120
<211> 11
<212> PRT
<213> Homo sapiens
```

```
<400> 120
Ser Gly Asp Lys Leu Gly Asn Lys Tyr Ala Ser
5 10
```

```
<210> 121
<211> 7
<212> PRT
<213> Homo sapiens
```

```
<400> 121
Gln Asp Ser Lys Arg Pro Ser
5
```

```
<210> 122
<211> 9
<212> PRT
<213> Homo sapiens
```

eolf-seql.txt

<400> 122  
Gln Ala Trp Asp Ser Thr Ile Val Val  
5

<210> 123  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 123  
Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Arg Gln  
5 10 15  
Thr Ala Ser Ile Thr Cys  
20

<210> 124  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 124  
Trp Tyr Gln Gln Lys Pro Gly His Ser Pro Val Leu Val Ile Tyr  
5 10 15

<210> 125  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 125  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr  
5 10 15  
Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Val Tyr Tyr Cys  
20 25 30

<210> 126  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 126  
Phe Gly Gly Gly Thr Lys Leu Thr Val Leu  
5 10

<210> 127  
<211> 351  
<212> DNA  
<213> Homo sapiens

<400> 127  
gagatacagc tgcaggagtc aggacctggc cttgtgaaac cttcacagtc actctccctc 60  
acctgttctg tcaactggta caccattacc agtgggttatg attggagctg gatccggaag 120  
ttcccaggaa ataaaatgga gtggatggga tacataagct acagtggtag cactaactac 180  
aaccatcgc tcaaaagtcg aatctccatt accagagaca catccaagaa tcagttcttc 240  
ctgcagttga actctgtaac tactgaggat acagccacat attactgtgc aagagggatg 300  
atggtactta ttcctaactg gggccaggga gtcatggtca cagtctcctc a 351

eolf-seql.txt

<210> 128  
 <211> 117  
 <212> PRT  
 <213> Homo sapiens

<400> 128  
 Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
                   5                  10                  15  
 Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr Ser Gly  
                   20                  25                  30  
 Tyr Asp Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
                   35                  40                  45  
 Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu  
                   50                  55                  60  
 Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe  
                   65                  70                  75                  80  
 Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys  
                   85                  90  
 Ala Arg Gly Met Met Val Leu Ile Pro Asn Trp Gly Gln Gly Val Met  
                   100                  105                  110  
 Val Thr Val Ser Ser  
                   115

<210> 129  
 <211> 4  
 <212> PRT  
 <213> Homo sapiens

<400> 129  
 Ser Gly Tyr Asp

<210> 130  
 <211> 18  
 <212> PRT  
 <213> Homo sapiens

<400> 130  
 Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu  
                   5                  10                  15  
 Lys Ser

<210> 131  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 131  
 Gly Met Met Val Leu Ile Pro Asn  
                   5

<210> 132  
 <211> 30

eolf-seql.txt

<212> PRT  
 <213> Homo sapiens  
 <400> 132  
 Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
                   5                  10                  15  
 Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr  
                   20                  25                  30

<210> 133  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens  
 <400> 133  
 Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
                   5                  10

<210> 134  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens  
 <400> 134  
 Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln  
                   5                  10                  15  
 Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 135  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens  
 <400> 135  
 Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
                   5                  10

<210> 136  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens  
 <400> 136  
 gatgtccaga tgaccagtc tccgtcttat cttactgcgt ctcttgagaga aagtgtttcc 60  
 atcagttgca aggcaagtaa gagcattact aattatttag cctgggtatca tcagaaacct 120  
 ggggaaccat ataaccttct tatctactct ggggtcaactt tgcaatctgg aactccatca 180  
 aggttcagtg gcagtagatc tggtagatc ttcatcttca ccatcagaag cctggagcct 240  
 gaagattttg gactctatta ctgtcaacag tattatgaaa aaccgtacac gtttggagct 300  
 gggaccaagc tggaactgaa a 321

<210> 137  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 137  
 Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Thr Ala Ser Pro Gly  
                   5                  10                  15  
 Glu Ser Val Ser Ile Ser Cys Lys Ala Ser Lys Ser Ile Thr Asn Tyr  
                   20                  25                  30  
 Leu Ala Trp Tyr His Gln Lys Pro Gly Glu Pro Tyr Asn Leu Leu Ile  
                   35                  40                  45  
 Tyr Ser Gly Ser Thr Leu Gln Ser Gly Thr Pro Ser Arg Phe Ser Gly  
                   50                  55                  60  
 Ser Arg Ser Gly Thr Asp Phe Ile Leu Thr Ile Arg Ser Leu Glu Pro  
                   65                  70                  75                  80  
 Glu Asp Phe Gly Leu Tyr Tyr Cys Gln Gln Tyr Tyr Glu Lys Pro Tyr  
                   85                  90                  95  
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
                   100                  105

<210> 138  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 138  
 Lys Ala Ser Lys Ser Ile Thr Asn Tyr Leu Ala  
                   5                  10

<210> 139  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 139  
 Ser Gly Ser Thr Leu Gln Ser  
                   5

<210> 140  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 140  
 Gln Gln Tyr Tyr Glu Lys Pro Tyr Thr  
                   5

<210> 141  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

<400> 141  
 Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Thr Ala Ser Pro Gly  
                   5                  10                  15  
 Glu Ser Val Ser Ile Ser Cys  
                   20

<210> 142  
 <211> 15

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 142  
Trp Tyr His Gln Lys Pro Gly Glu Pro Tyr Asn Leu Leu Ile Tyr  
5 10 15

<210> 143  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 143  
Gly Thr Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Ile  
5 10 15  
Leu Thr Ile Arg Ser Leu Glu Pro Glu Asp Phe Gly Leu Tyr Tyr Cys  
20 25 30

<210> 144  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 144  
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
5 10

<210> 163  
<211> 363  
<212> DNA  
<213> Homo sapiens

<400> 163  
caggtcaacc tactgcagtc tggggctgca ctggtgaagc ctggggcctc tgtgaagttg 60  
tcttgcaaag cctctgggta tacattcact gactactata tacactgggt gaagcagagt 120  
catggaatga gccttgagtg gattgggctt attaatcctg acagtgggta tcctaactac 180  
aatgaaaatt tcaagggcaa ggccacattg actgttgaca aatccaccaa tacagcctat 240  
atggagcttc gcagattgac atctgaggac tctgcaacct attactgtac aagatcgagg 300  
atttactatg atgggttcggt ttttgattac tggggccaag gagtcatggt cacagtcctc 360  
tca 363

<210> 164  
<211> 121  
<212> PRT  
<213> Homo sapiens

<400> 164  
Gln Val Asn Leu Leu Gln Ser Gly Ala Ala Leu Val Lys Pro Gly Ala  
5 10 15  
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr  
20 25 30

Tyr Ile His Trp Val Lys Gln Ser His Gly Met Ser Leu Glu Trp Ile  
Page 31

eolf-seql.txt

35 40 45  
 Gly Leu Ile Asn Pro Asp Ser Gly Tyr Pro Asn Tyr Asn Glu Asn Phe  
 50 55 60  
 Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn Thr Ala Tyr  
 65 70 75 80  
 Met Glu Leu Arg Arg Leu Thr Ser Glu Asp Ser Ala Thr Tyr Tyr Cys  
 85 90 95  
 Thr Arg Ser Arg Ile Tyr Tyr Asp Gly Ser Val Phe Asp Tyr Trp Gly  
 100 105 110  
 Gln Gly Val Met Val Thr Val Ser Ser  
 115 120

<210> 165  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 165  
 Asp Tyr Tyr Ile His  
 5

<210> 166  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 166  
 Leu Ile Asn Pro Asp Ser Gly Tyr Pro Asn Tyr Asn Glu Asn Phe Lys  
 5 10 15

Gly

<210> 167  
 <211> 12  
 <212> PRT  
 <213> Homo sapiens

<400> 167  
 Ser Arg Ile Tyr Tyr Asp Gly Ser Val Phe Asp Tyr  
 5 10

<210> 168  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 168  
 Gln Val Asn Leu Leu Gln Ser Gly Ala Ala Leu Val Lys Pro Gly Ala  
 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr  
 20 25 30

<210> 169  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 169  
Trp Val Lys Gln Ser His Gly Met Ser Leu Glu Trp Ile Gly  
5 10

<210> 170  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 170  
Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn Thr Ala Tyr Met Glu  
5 10 15  
Leu Arg Arg Leu Thr Ser Glu Asp Ser Ala Thr Tyr Tyr Cys Thr Arg  
20 25 30

<210> 171  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 171  
Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
5 10

<210> 172  
<211> 318  
<212> DNA  
<213> Homo sapiens

<400> 172  
gaaattgtgc taaccagtc tccaacaacc atggctgtat ctccggggga gaaggtcacc 60  
atcacctgcc gtgccaggtc cagtgtaacg tacatgtact ggtaccagca gaagtcaggc 120  
gcctccccta aaccctggat ttatgaaaca tccaaactgg cttctggagt cccagatcgc 180  
ttcagtggca gtgggtctgg gacctcttat tcgttcacaa tcagctccat ggagactgaa 240  
gatgctgcca cttattattg tcaccagtgg agtaggaccc caccacggtt tggaggtggg 300  
accaagctgg aaatgaga 318

<210> 173  
<211> 106  
<212> PRT  
<213> Homo sapiens

<400> 173  
Glu Ile Val Leu Thr Gln Ser Pro Thr Thr Met Ala Val Ser Pro Gly  
5 10 15  
Glu Lys Val Thr Ile Thr Cys Arg Ala Arg Ser Ser Val Ser Tyr Met  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Ser Gly Ala Ser Pro Lys Pro Trp Ile Tyr  
35 40 45  
Glu Thr Ser Lys Leu Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Ser Tyr Ser Phe Thr Ile Ser Ser Met Glu Thr Glu  
65 70 75 80

eolf-seql.txt

Asp Ala Ala Thr Tyr Tyr Cys His Gln Trp Ser Arg Thr Pro Pro Thr  
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Met Arg  
100 105

<210> 174  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 174  
Arg Ala Arg Ser Ser Val Ser Tyr Met Tyr  
5 10

<210> 175  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 175  
Glu Thr Ser Lys Leu Ala Ser  
5

<210> 176  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 176  
His Gln Trp Ser Arg Thr Pro Pro Thr  
5

<210> 177  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 177  
Glu Ile Val Leu Thr Gln Ser Pro Thr Thr Met Ala Val Ser Pro Gly  
5 10 15

Glu Lys Val Thr Ile Thr Cys  
20

<210> 178  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 178  
Trp Tyr Gln Gln Lys Ser Gly Ala Ser Pro Lys Pro Trp Ile Tyr  
5 10 15

<210> 179  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 179  
Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser

eof-seq1.txt

5

10

15

Phe Thr Ile Ser Ser Met Glu Thr Glu Asp Ala Ala Thr Tyr Tyr Cys  
20 25 30

<210> 180  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 180  
Phe Gly Gly Gly Thr Lys Leu Glu Met Arg  
5 10

<210> 181  
<211> 351  
<212> DNA  
<213> Homo sapiens

<400> 181  
gagatacagc tgcaggagtc aggacctggc cttgtgaaac cttcacagtc actctccctc 60  
acctgttctg tcaactggta caccattacc agcggttatg attggagctg gatccggaag 120  
ttcccaggaa ataaaatgga gtggatggga tacataagct acagtggtaa cactaactac 180  
aaccatcgc tcaaaagtcg aatctccatt accagagaca catccaagaa tcagttcttc 240  
ctgcagttga actctgttac tactgaggat atagccacat attactgtgg aagagggatg 300  
gtggtacttg ttagtacctg gggccaagga gtcatggtca cagtctcctc a 351

<210> 182  
<211> 117  
<212> PRT  
<213> Homo sapiens

<400> 182  
Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
5 10 15  
Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr Ser Gly  
20 25 30  
Tyr Asp Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
35 40 45  
Met Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu  
50 55 60  
Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe  
65 70 75 80  
Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Ile Ala Thr Tyr Tyr Cys  
85 90 95  
Gly Arg Gly Met Val Val Leu Val Ser Thr Trp Gly Gln Gly Val Met  
100 105 110  
Val Thr Val Ser Ser  
115

<210> 183  
<211> 4

<212> PRT  
 <213> Homo sapiens

<400> 183  
 Ser Gly Tyr Asp

<210> 184  
 <211> 18  
 <212> PRT  
 <213> Homo sapiens

<400> 184  
 Met Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu  
                   5                  10                  15

Lys Ser

<210> 185  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 185  
 Gly Met Val Val Leu Val Ser Thr  
                   5

<210> 186  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 186  
 Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
                   5                  10                  15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr  
                   20                  25                  30

<210> 187  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 187  
 Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
                   5                  10

<210> 188  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 188  
 Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln  
                   5                  10                  15

Leu Asn Ser Val Thr Thr Glu Asp Ile Ala Thr Tyr Tyr Cys Gly Arg  
                   20                  25                  30

<210> 189

eolf-seql.txt

<211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 189  
 Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
                   5                  10

<210> 190  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 190  
 gatgtccaga tgaccagtc tccgtcttat cttgctgcgt ctcttgagaga aagtgtttcc 60  
 atcagttgca agacaagtaa gagcattacc cattatttag cctgggtatca acagaagcct 120  
 ggggaagcat ttaaacttct tatctattct ggggtcaactt tgcaatctgg aactccatca 180  
 aggttcattg gcagtggagc tgttacagat ttcactctca ccatcagaag cctggagcct 240  
 gaagattttg gactctatta ctgtcaacag tattatgaaa acccgtagac gtttggagct 300  
 gggaccaagc tggaactgaa a 321

<210> 191  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 191  
 Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
                   5                  10                  15  
 Glu Ser Val Ser Ile Ser Cys Lys Thr Ser Lys Ser Ile Thr His Tyr  
                   20                  25                  30  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Glu Ala Phe Lys Leu Leu Ile  
                   35                  40                  45  
 Tyr Ser Gly Ser Thr Leu Gln Ser Gly Thr Pro Ser Arg Phe Ile Gly  
                   50                  55                  60  
 Ser Gly Ala Val Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Glu Pro  
                   65                  70                  75                  80  
 Glu Asp Phe Gly Leu Tyr Tyr Cys Gln Gln Tyr Tyr Glu Asn Pro Tyr  
                   85                  90                  95  
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
                   100                  105

<210> 192  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 192  
 Lys Thr Ser Lys Ser Ile Thr His Tyr Leu Ala  
                   5                  10

<210> 193  
 <211> 7

<212> PRT  
 <213> Homo sapiens

<400> 193  
 Ser Gly Ser Thr Leu Gln Ser  
 5

<210> 194  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 194  
 Gln Gln Tyr Tyr Glu Asn Pro Tyr Thr  
 5

<210> 195  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

<400> 195  
 Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
 5 10 15  
 Glu Ser Val Ser Ile Ser Cys  
 20

<210> 196  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 196  
 Trp Tyr Gln Gln Lys Pro Gly Glu Ala Phe Lys Leu Leu Ile Tyr  
 5 10 15

<210> 197  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 197  
 Gly Thr Pro Ser Arg Phe Ile Gly Ser Gly Ala Val Thr Asp Phe Thr  
 5 10 15  
 Leu Thr Ile Arg Ser Leu Glu Pro Glu Asp Phe Gly Leu Tyr Tyr Cys  
 20 25 30

<210> 198  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 198  
 Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
 5 10

<210> 217

eolf-seql.txt

<211> 372  
<212> DNA  
<213> Homo sapiens

<400> 217  
caggttactc tgaagagtc tggccctggg atattgcagc cttcccagac cctcagtctg 60  
acttgctctt tctctgggtt ttcactgagc acttttggtt tatgtgtgag ctggattcgt 120  
cagccttcag ggaagggctt ggagtggctg gcaattatct gttgggagga tagtaagggc 180  
tacaaccctt ctctgaagaa ccggctcaca atctccaagg acacctcaa caaccaagca 240  
ttcctcaaga tctccagtgt ggacactgca gataccgcca tatactactg tgctcggagg 300  
tccgttatgt atactacggc cccgtactac tttgattact ggggccaagg agtcatgggc 360  
acagtctcct ca 372

<210> 218  
<211> 124  
<212> PRT  
<213> Homo sapiens

<400> 218  
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln  
5 10 15  
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Phe  
20 25 30  
Gly Ile Cys Val Ser Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu  
35 40 45  
Trp Leu Ala Ile Ile Cys Trp Glu Asp Ser Lys Gly Tyr Asn Pro Ser  
50 55 60  
Leu Lys Asn Arg Leu Thr Ile Ser Lys Asp Thr Ser Asn Asn Gln Ala  
65 70 75 80  
Phe Leu Lys Ile Ser Ser Val Asp Thr Ala Asp Thr Ala Ile Tyr Tyr  
85 90 95  
Cys Ala Arg Arg Ser Val Met Tyr Thr Thr Ala Pro Tyr Tyr Phe Asp  
100 105 110  
Tyr Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
115 120

<210> 219  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 219  
Thr Phe Gly Ile Cys Val Ser  
5

<210> 220  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 220  
Ile Ile Cys Trp Glu Asp Ser Lys Gly Tyr Asn Pro Ser Leu Lys Asn

<210> 221  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 221  
 Arg Ser Val Met Tyr Thr Thr Ala Pro Tyr Tyr Phe Asp Tyr  
                   5                                  10

<210> 222  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 222  
 Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln  
                   5                                  10                  15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser  
                   20                                  25                  30

<210> 223  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 223  
 Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu Trp Leu Ala  
                   5                                  10

<210> 224  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 224  
 Arg Leu Thr Ile Ser Lys Asp Thr Ser Asn Asn Gln Ala Phe Leu Lys  
                   5                                  10                  15

Ile Ser Ser Val Asp Thr Ala Asp Thr Ala Ile Tyr Tyr Cys Ala Arg  
                   20                                  25                  30

<210> 225  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 225  
 Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
                   5                                  10

<210> 226  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 226  
 gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga aattgtcacc 60

atcacatgcc aggcaagcca agacattggt aattggttgg catggtttca gcagaaaccg 120

eolf-seql.txt

```

gggaaatctc ctcagctcct gatttatgat gcaaccacct tggcagatgg ggtcccatca    180
cggttcagcg gcagtagatc tggcacacag ttttctctta agatcaacag attacagggtt    240
gaagatattg gaagctatta ctgtcaacag gctcataata atccgaacac gtttggacgg    300
gggaccaagc tggaaatgaa a                                              321

```

```

<210>    227
<211>    107
<212>    PRT
<213>    Homo sapiens

```

```

<400>    227
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu
                    5                      10                      15

Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp
                    20                      25                      30

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
                    35                      40                      45

Tyr Asp Ala Thr Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
                    50                      55                      60

Ser Arg Ser Gly Thr Gln Phe Ser Leu Lys Ile Asn Arg Leu Gln Val
                    65                      70                      75                      80

Glu Asp Ile Gly Ser Tyr Tyr Cys Gln Gln Ala His Asn Asn Pro Asn
                    85                      90                      95

Thr Phe Gly Arg Gly Thr Lys Leu Glu Met Lys
                    100                     105

```

```

<210>    228
<211>     11
<212>    PRT
<213>    Homo sapiens

```

```

<400>    228
Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala
                    5                      10

```

```

<210>    229
<211>      7
<212>    PRT
<213>    Homo sapiens

```

```

<400>    229
Asp Ala Thr Thr Leu Ala Asp
                    5

```

```

<210>    230
<211>      9
<212>    PRT
<213>    Homo sapiens

```

```

<400>    230
Gln Gln Ala His Asn Asn Pro Asn Thr
                    5

```

eolf-seql.txt

<210> 231  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

<400> 231  
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
                   5                  10                  15  
 Glu Ile Val Thr Ile Thr Cys  
                   20

<210> 232  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 232  
 Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile Tyr  
                   5                  10                  15

<210> 233  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 233  
 Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Phe Ser  
                   5                  10                  15  
 Leu Lys Ile Asn Arg Leu Gln Val Glu Asp Ile Gly Ser Tyr Tyr Cys  
                   20                  25                  30

<210> 234  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 234  
 Phe Gly Arg Gly Thr Lys Leu Glu Met Lys  
                   5                  10

<210> 244  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 244  
 gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga aattgtcacc 60  
 atcacatgcc aggcaagcca agacattggg aattgggttg catggtatca gcagaaaccg 120  
 gggaaatctc ctgagctcct gctttatgat gcaaccagct tggcagatgg ggtcccatca 180  
 cggttcagcg gcagtagatc tggcacacag tattctctta agatcagcag actacagggt 240  
 gaagatattg gaagctatta ctgtcaacag gctcatagta atccttggac gttcgggtgga 300  
 ggcaccaagc tggaattgaa a 321

<210> 245  
 <211> 107  
 <212> PRT

eolf-seql.txt

```

<213> Homo sapiens
<400> 245
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu
          5          10          15
Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp
          20          25          30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Leu
          35          40          45
Tyr Asp Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
          50          55          60
Ser Arg Ser Gly Thr Gln Tyr Ser Leu Lys Ile Ser Arg Leu Gln Val
          65          70          75          80
Glu Asp Ile Gly Ser Tyr Tyr Cys Gln Gln Ala His Ser Asn Pro Trp
          85          90          95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
          100          105

```

```

<210> 246
<211> 11
<212> PRT
<213> Homo sapiens

```

```

<400> 246
Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala
          5          10

```

```

<210> 247
<211> 7
<212> PRT
<213> Homo sapiens

```

```

<400> 247
Asp Ala Thr Ser Leu Ala Asp
          5

```

```

<210> 248
<211> 9
<212> PRT
<213> Homo sapiens

```

```

<400> 248
Gln Gln Ala His Ser Asn Pro Trp Thr
          5

```

```

<210> 249
<211> 23
<212> PRT
<213> Homo sapiens

```

```

<400> 249
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu
          5          10          15
Glu Ile Val Thr Ile Thr Cys
          20

```

eolf-seql.txt

<210> 250  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 250  
Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Leu Tyr  
5 10 15

<210> 251  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 251  
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Tyr Ser  
5 10 15  
Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ser Tyr Tyr Cys  
20 25 30

<210> 252  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 252  
Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
5 10

<210> 253  
<211> 351  
<212> DNA  
<213> Homo sapiens

<400> 253  
gagatacagc tgcaggagtc aggacctggc cttgtgaaac cttcacagtc actctccctc 60  
acctgttctg tcaactggta caccattacc agtgggttatg attggagctg gatccggaag 120  
ttcccaggaa ataaaatgga gtggatggga tacataagct acagtggtag cactaactac 180  
aaccatcgc tcaaaagtcg aatctccatt accagagaca catccaagaa tcagttcttc 240  
ctgcagttga actctgttac tactgaggat atagccacat attactgtgc aagagggatg 300  
atggtactta ttagtaactg gggccaagga gtcatggtca cagtctcctc a 351

<210> 254  
<211> 117  
<212> PRT  
<213> Homo sapiens

<400> 254  
Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
5 10 15  
Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr Ser Gly  
20 25 30  
Tyr Asp Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
35 40 45

Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu  
Page 44

eolf-seql.txt

50

55

60

Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe  
65 70 75 80  
Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Ile Ala Thr Tyr Tyr Cys  
85 90 95  
Ala Arg Gly Met Met Val Leu Ile Ser Asn Trp Gly Gln Gly Val Met  
100 105 110  
Val Thr Val Ser Ser  
115

<210> 255  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 255  
Ser Gly Tyr Asp

<210> 256  
<211> 18  
<212> PRT  
<213> Homo sapiens

<400> 256  
Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu  
5 10 15

Lys Ser

<210> 257  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 257  
Gly Met Met Val Leu Ile Ser Asn  
5

<210> 258  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 258  
Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
5 10 15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr  
20 25 30

<210> 259  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 259  
Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Lys Met Glu Trp

<210> 260  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 260  
 Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln  
                     5                    10                    15  
 Leu Asn Ser Val Thr Thr Glu Asp Ile Ala Thr Tyr Tyr Cys Ala Arg  
                     20                    25                    30

<210> 261  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 261  
 Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
                     5                    10

<210> 262  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 262  
 gatgtccaga tgaccagtc tccgtcttat cttgctgcgt ctcttgagaga aagtgtttcc 60  
 atcagttgca aggcaagtaa gagcattact cattatttag cctggatatca acagaagcct 120  
 ggggaagcat ataaacttct tatctactct ggggtcaactt tgcaatctgg aactccatca 180  
 aggttcattg gcaactggagc tggtacagat ttcactctca ccatcagaag cctggagcct 240  
 gaagattttg gactctatta ctgtcaacag tattatgaaa aaccgtacac gtttggagct 300  
 gggaccaagc tggaactgaa a 321

<210> 263  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 263  
 Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
                     5                    10                    15  
 Glu Ser Val Ser Ile Ser Cys Lys Ala Ser Lys Ser Ile Thr His Tyr  
                     20                    25                    30  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Glu Ala Tyr Lys Leu Leu Ile  
                     35                    40                    45  
 Tyr Ser Gly Ser Thr Leu Gln Ser Gly Thr Pro Ser Arg Phe Ile Gly  
                     50                    55                    60  
 Thr Gly Ala Val Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Glu Pro  
                     65                    70                    75                    80  
 Glu Asp Phe Gly Leu Tyr Tyr Cys Gln Gln Tyr Tyr Glu Lys Pro Tyr  
                     85                    90                    95

eolf-seql.txt

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
100 105

<210> 264  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 264  
Lys Ala Ser Lys Ser Ile Thr His Tyr Leu Ala  
5 10

<210> 265  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 265  
Ser Gly Ser Thr Leu Gln Ser  
5

<210> 266  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 266  
Gln Gln Tyr Tyr Glu Lys Pro Tyr Thr  
5

<210> 267  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 267  
Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
5 10 15

Glu Ser Val Ser Ile Ser Cys  
20

<210> 268  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 268  
Trp Tyr Gln Gln Lys Pro Gly Glu Ala Tyr Lys Leu Leu Ile Tyr  
5 10 15

<210> 269  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 269  
Gly Thr Pro Ser Arg Phe Ile Gly Thr Gly Ala Val Thr Asp Phe Thr  
5 10 15

Leu Thr Ile Arg Ser Leu Glu Pro Glu Asp Phe Gly Leu Tyr Tyr Cys  
Page 47

20

25

30

<210> 270  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 270  
 Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
                   5                                  10

<210> 271  
 <211> 357  
 <212> DNA  
 <213> Homo sapiens

<400> 271  
 caggtgcagc tgaaggagtc aggacctggt ctggtgcagc cctcacagac cctgtccctc 60  
 acctgcactg tctctgggtt ctactaacc cgctatgatg tgcactgggt tcgccagcct 120  
 ccaggaaagg gtctggagtg gatgggagga atatggggtg atggaagcac agattataat 180  
 tcagctctca aatcccgact gagcatcagc agggacacct ccaagagtca agtgttctta 240  
 aaaatgaaca gtctgcaaac tgaagacaca gccatttact tctgtaccag atctctggac 300  
 tacagtgggtg acggggtttgg ttattggggc caaggcactc tggtcactgt ctcttca 357

<210> 272  
 <211> 119  
 <212> PRT  
 <213> Homo sapiens

<400> 272  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Gln Pro Ser Gln  
                   5                                  10                                  15  
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Arg Tyr  
                   20                                  25                                  30  
 Asp Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met  
                   35                                  40                                  45  
 Gly Gly Ile Trp Gly Asp Gly Ser Thr Asp Tyr Asn Ser Ala Leu Lys  
                   50                                  55                                  60  
 Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu  
                   65                                  70                                  75                                  80  
 Lys Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Ile Tyr Phe Cys Thr  
                   85                                  90                                  95  
 Arg Ser Leu Asp Tyr Ser Gly Asp Gly Phe Gly Tyr Trp Gly Gln Gly  
                   100                                  105                                  110  
 Thr Leu Val Thr Val Ser Ser  
                   115

<210> 273  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 273  
Arg Tyr Asp Val His  
5

<210> 274  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 274  
Gly Ile Trp Gly Asp Gly Ser Thr Asp Tyr Asn Ser Ala Leu Lys Ser  
5 10 15

<210> 275  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 275  
Ser Leu Asp Tyr Ser Gly Asp Gly Phe Gly Tyr  
5 10

<210> 276  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 276  
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Gln Pro Ser Gln  
5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
20 25 30

<210> 277  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 277  
Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
5 10

<210> 278  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 278  
Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu Lys  
5 10 15

Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Ile Tyr Phe Cys Thr Arg  
20 25 30

<210> 279  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 279  
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

<210> 280  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 280  
 gacatccaga tgacacagtc tcctccctcc ctgtctgcat ctctgggaga caaagtcacc 60  
 atcacttgcc aggcaagtca aaacattaac aagtatatag cttggtatca gcaaaagcct 120  
 ggaaaagctc ctaggcagct catacgttac acatctgcac tagtgtcagg cacctcatcg 180  
 aggttcagtg gcagtggatc tgggagagat tattcattca gcatcagcaa cgtggagtct 240  
 gaagatattg caagttatta ctgtctacag tacgataacc ttccgtacac atttgagct 300  
 gggaccaagc tggaactgaa a 321

<210> 281  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 281  
 Asp Ile Gln Met Thr Gln Ser Pro Pro Ser Leu Ser Ala Ser Leu Gly  
                   5                  10                  15  
 Asp Lys Val Thr Ile Thr Cys Gln Ala Ser Gln Asn Ile Asn Lys Tyr  
                   20                  25                  30  
 Ile Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Gln Leu Ile  
                   35                  40                  45  
 Arg Tyr Thr Ser Ala Leu Val Ser Gly Thr Ser Ser Arg Phe Ser Gly  
                   50                  55                  60  
 Ser Gly Ser Gly Arg Asp Tyr Ser Phe Ser Ile Ser Asn Val Glu Ser  
                   65                  70                  75                  80  
 Glu Asp Ile Ala Ser Tyr Tyr Cys Leu Gln Tyr Asp Asn Leu Pro Tyr  
                   85                  90                  95  
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
                   100                  105

<210> 282  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 282  
 Gln Ala Ser Gln Asn Ile Asn Lys Tyr Ile Ala  
                   5                  10

<210> 283  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 283  
 Tyr Thr Ser Ala Leu Val Ser  
                   5

eolf-seql.txt

<210> 284  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 284  
 Leu Gln Tyr Asp Asn Leu Pro Tyr Thr  
 5

<210> 285  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

<400> 285  
 Asp Ile Gln Met Thr Gln Ser Pro Pro Ser Leu Ser Ala Ser Leu Gly  
 5 10 15  
 Asp Lys Val Thr Ile Thr Cys  
 20

<210> 286  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 286  
 Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Gln Leu Ile Arg  
 5 10 15

<210> 287  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 287  
 Gly Thr Ser Ser Arg Phe Ser Gly Ser Gly Ser Gly Arg Asp Tyr Ser  
 5 10 15  
 Phe Ser Ile Ser Asn Val Glu Ser Glu Asp Ile Ala Ser Tyr Tyr Cys  
 20 25 30

<210> 288  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 288  
 Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
 5 10

<210> 289  
 <211> 360  
 <212> DNA  
 <213> Homo sapiens

<400> 289  
 caggttactc tgaaagagtc tggccctggg atattgcagc cttcccagac cctcagtcctg 60  
 acttgctctt tctctggggtt ttactgaac acttatggta tatgtgtgag ctggattcgt 120

eolf-seql.txt

cagccttcag ggaaggggtct ggagtggctg gcaactatatt gttgggagga tagtaaggtc 180  
 tacaaccctt ctctgaagaa ccggctcaca atctccaagg acacctccaa caaccaagca 240  
 ttctcaaga tcaccagtgt ggacactgca gataccgcca tatactactg tgctcggagg 300  
 agggtttggg catactactt tgattactgg ggccaaggag tcatgggtcac agtctctca 360

<210> 290  
 <211> 120  
 <212> PRT  
 <213> Homo sapiens

<400> 290  
 Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln  
                   5                  10                  15  
 Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Asn Thr Tyr  
           20                  25                  30  
 Gly Ile Cys Val Ser Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu  
           35                  40                  45  
 Trp Leu Ala Thr Ile Cys Trp Glu Asp Ser Lys Val Tyr Asn Pro Ser  
       50                  55                  60  
 Leu Lys Asn Arg Leu Thr Ile Ser Lys Asp Thr Ser Asn Asn Gln Ala  
 65                  70                  75                  80  
 Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Ile Tyr Tyr  
           85                  90                  95  
 Cys Ala Arg Arg Arg Val Trp Ser Tyr Tyr Phe Asp Tyr Trp Gly Gln  
           100                  105                  110  
 Gly Val Met Val Thr Val Ser Ser  
       115                  120

<210> 291  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 291  
 Thr Tyr Gly Ile Cys Val Ser  
                   5

<210> 292  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 292  
 Thr Ile Cys Trp Glu Asp Ser Lys Val Tyr Asn Pro Ser Leu Lys Asn  
           5                  10                  15

<210> 293  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 293  
 Arg Arg Val Trp Ser Tyr Tyr Phe Asp Tyr  
           5                  10

eolf-seql.txt

<210> 294  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 294  
 Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln  
                   5                  10                  15  
 Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Asn  
                   20                  25                  30

<210> 295  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 295  
 Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu Trp Leu Ala  
                   5                  10

<210> 296  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 296  
 Arg Leu Thr Ile Ser Lys Asp Thr Ser Asn Asn Gln Ala Phe Leu Lys  
                   5                  10                  15  
 Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Ile Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 297  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 297  
 Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
                   5                  10

<210> 298  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 298  
 gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga aattgtcacc 60  
 atcacatgcc aggcaagcca agacattggg aattgggttg catggtatca gcagaaaccg 120  
 gggaaatctc ctcagctcct gatttatgat gcaaccagct tggcagatgg ggtcccatca 180  
 cggttcagcg gcagtagatc tggcacacag tattctctta agatcagcag actacaggtt 240  
 gaagatattg gaagctatta ctgtcaacag gctcatacta atccgctcac gttcggttct 300  
 gggaccaagc tggagatcaa a 321

<210> 299

eolf-seql.txt

<211> 107  
<212> PRT  
<213> Homo sapiens

<400> 299  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15  
Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp  
20 25 30  
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile  
35 40 45  
Tyr Asp Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly  
50 55 60  
Ser Arg Ser Gly Thr Gln Tyr Ser Leu Lys Ile Ser Arg Leu Gln Val  
65 70 75 80  
Glu Asp Ile Gly Ser Tyr Tyr Cys Gln Gln Ala His Thr Asn Pro Leu  
85 90 95  
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys  
100 105

<210> 300  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 300  
Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala  
5 10

<210> 301  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 301  
Asp Ala Thr Ser Leu Ala Asp  
5

<210> 302  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 302  
Gln Gln Ala His Thr Asn Pro Leu Thr  
5

<210> 303  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 303  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15  
Glu Ile Val Thr Ile Thr Cys  
20

eolf-seql.txt

<210> 304  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 304  
 Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile Tyr  
           5                  10                  15

<210> 305  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 305  
 Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Tyr Ser  
           5                  10  
 Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ser Tyr Tyr Cys  
           20                  25                  30

<210> 306  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 306  
 Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys  
           5                  10

<210> 307  
 <211> 351  
 <212> DNA  
 <213> Homo sapiens

<400> 307  
 gagatacagc tgcaggagtc aggacctggc cttgtgaaac cttcacagtc actctccctc 60  
 acctgttctg tcaactggta caccattacc agtgggttttg attggagctg gttccggaag 120  
 ttcccaggaa ataaaatgga gtggatggga tacataagct acagtggtag cactaactac 180  
 aacccatcgc tcaaaagtcg aatctccatt accagagaca catccaagaa tcagttcttc 240  
 ctgcagttga actctgtaac tactgaagat acagccacat attactgtgc aagagggggtc 300  
 tcctccctgt ctgcttactg gggccaaggc actctggtca ctgtctcttc a 351

<210> 308  
 <211> 117  
 <212> PRT  
 <213> Homo sapiens

<400> 308  
 Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
           5                  10                  15  
 Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr Ser Gly  
           20                  25                  30  
 Phe Asp Trp Ser Trp Phe Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
           35                  40                  45

eolf-seql.txt

Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu  
50 55 60  
Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe  
65 70 75 80  
Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys  
85 90 95  
Ala Arg Gly Val Ser Ser Leu Ser Ala Tyr Trp Gly Gln Gly Thr Leu  
100 105 110  
Val Thr Val Ser Ser  
115

<210> 309  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 309  
Ser Gly Phe Asp

<210> 310  
<211> 18  
<212> PRT  
<213> Homo sapiens

<400> 310  
Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu  
5 10 15

Lys Ser

<210> 311  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 311  
Gly Val Ser Ser Leu Ser Ala Tyr  
5

<210> 312  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 312  
Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
5 10 15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr  
20 25 30

<210> 313  
<211> 14  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 313  
Trp Ser Trp Phe Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
5 10

<210> 314  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 314  
Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln  
5 10 15  
Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
20 25 30

<210> 315  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 315  
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 316  
<211> 321  
<212> DNA  
<213> Homo sapiens

<400> 316  
gatgtccaga tgaccagtc tccgtcttat cttgctgcgt ctcctggaga gagggtttcc 60  
atcagttgca aggcaagtaa gctcattact aattatttag cctggatatca acagaaacct 120  
ggggaaccat ataaccttct tatctactct ggggtcaactt tgcaatctgg cactccatca 180  
aggttcagtg gcagtagatc tggtagacat ttcactctca ccatcagaag cctgcagcct 240  
gaagattttg gactctatta ctgtcaacag tattatgaaa aaccgtacac gtttggaggt 300  
gggaccaagc tggaactgaa a 321

<210> 317  
<211> 107  
<212> PRT  
<213> Homo sapiens

<400> 317  
Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
5 10 15  
Glu Ser Val Ser Ile Ser Cys Lys Ala Ser Lys Leu Ile Thr Asn Tyr  
20 25 30  
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Glu Pro Tyr Asn Leu Leu Ile  
35 40 45  
Tyr Ser Gly Ser Thr Leu Gln Ser Gly Thr Pro Ser Arg Phe Ser Gly  
50 55 60  
Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro  
65 70 75 80

eolf-seql.txt

Glu Asp Phe Gly Leu Tyr Tyr Cys Gln Gln Tyr Tyr Glu Lys Pro Tyr  
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
100 105

<210> 318  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 318  
Lys Ala Ser Lys Leu Ile Thr Asn Tyr Leu Ala  
5 10

<210> 319  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 319  
Ser Gly Ser Thr Leu Gln Ser  
5

<210> 320  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 320  
Gln Gln Tyr Tyr Glu Lys Pro Tyr Thr  
5

<210> 321  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 321  
Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
5 10 15

Glu Ser Val Ser Ile Ser Cys  
20

<210> 322  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 322  
Trp Tyr Gln Gln Lys Pro Gly Glu Pro Tyr Asn Leu Leu Ile Tyr  
5 10 15

<210> 323  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 323  
Gly Thr Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr  
5 10 15

eolf-seql.txt

Leu Thr Ile Arg Ser Leu Gln Pro Glu Asp Phe Gly Leu Tyr Tyr Cys  
 20 25 30

<210> 324  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 324  
 Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
 5 10

<210> 325  
 <211> 366  
 <212> DNA  
 <213> Homo sapiens

<400> 325  
 caggtgcagc tgaaggagtc aggacctggc ctggtgaagc cctcagagac cctgtctctc 60  
 acctgcactg tctctgggtt ctcattaacc agctatcatg taagctgggt tcgacagcct 120  
 ccaggaaagg gtctggagtg gatgggaata atatggggtg atggaagcac agcatataat 180  
 tcagctctca aatcccgact gagcatcagc agggacacct cgaagagcca agttttctta 240  
 aaaatgaaca gtctgcaaac tgaagacaca gccacttact actgtgtcag agccggacat 300  
 tattctgatg gtagttatta ctacggggct tactggggcc aaggcactct ggtcactgtc 360  
 tcttca 366

<210> 326  
 <211> 122  
 <212> PRT  
 <213> Homo sapiens

<400> 326  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
 5 10 15  
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Tyr  
 20 25 30  
 His Val Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met  
 35 40 45  
 Gly Ile Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys  
 50 55 60  
 Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu  
 65 70 75 80  
 Lys Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Val  
 85 90 95  
 Arg Ala Gly His Tyr Ser Asp Gly Ser Tyr Tyr Tyr Gly Ala Tyr Trp  
 100 105 110  
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120

<210> 327

eolf-seql.txt

<211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 327  
 Ser Tyr His Val Ser  
 5

<210> 328  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 328  
 Ile Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys Ser  
 5 10 15

<210> 329  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 329  
 Ala Gly His Tyr Ser Asp Gly Ser Tyr Tyr Tyr Gly Ala Tyr  
 5 10

<210> 330  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 330  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
 5 10 15  
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
 20 25 30

<210> 331  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 331  
 Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
 5 10

<210> 332  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 332  
 Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu Lys  
 5 10 15  
 Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Val Arg  
 20 25 30

<210> 333  
 <211> 11  
 <212> PRT

<213> Homo sapiens

<400> 333  
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 334  
<211> 321  
<212> DNA  
<213> Homo sapiens

<400> 334  
gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga gattgtcacc 60  
atcacatgcc aggcaagcca agacattggt aattggttgg catggtatca gcagaagccg 120  
gggaaatctc ctcagctcct gatttatgat gcaaccacct tggcagatgg ggtcccatca 180  
cggttcagcg gcagtagatc tggcacacag tattctctta agatcagcag actacaggtt 240  
gaagatattg gaagctatta ctgtcaacag actcatagtc atcctcggac gttcgggtgga 300  
ggcaccaacc tggaattgaa a 321

<210> 335  
<211> 107  
<212> PRT  
<213> Homo sapiens

<400> 335  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15  
Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp  
20 25 30  
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile  
35 40 45  
Tyr Asp Ala Thr Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly  
50 55 60  
Ser Arg Ser Gly Thr Gln Tyr Ser Leu Lys Ile Ser Arg Leu Gln Val  
65 70 75 80  
Glu Asp Ile Gly Ser Tyr Tyr Cys Gln Gln Thr His Ser His Pro Arg  
85 90 95  
Thr Phe Gly Gly Gly Thr Asn Leu Glu Leu Lys  
100 105

<210> 336  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 336  
Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala  
5 10

<210> 337  
<211> 7  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 337  
Asp Ala Thr Thr Leu Ala Asp  
5

<210> 338  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 338  
Gln Gln Thr His Ser His Pro Arg Thr  
5

<210> 339  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 339  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15  
Glu Ile Val Thr Ile Thr Cys  
20

<210> 340  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 340  
Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile Tyr  
5 10 15

<210> 341  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 341  
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Tyr Ser  
5 10 15  
Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ser Tyr Tyr Cys  
20 25 30

<210> 342  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 342  
Phe Gly Gly Gly Thr Asn Leu Glu Leu Lys  
5 10

<210> 343  
<211> 351  
<212> DNA  
<213> Homo sapiens

<400> 343

eolf-seql.txt

gagatacagc tgcaggagtc aggacctggc cttgtgaaac cttcacagtc actctccctc 60  
acctgttctg tcaactggta caccattacc agtgggtttg attggagctg gttccggaag 120  
ttcccaggaa ataaaatgga gtggatggga tacattagct acagtgggat cactaactac 180  
aaccatcgc tcaaaagtcg aatctccatt accagagaca catccaagaa tcagttcttc 240  
ctgcagttga actctgtaac tactgaagat acagccacat attactgtgc aagaggggtc 300  
tcctccctgt ctgcttactg gggccaaggc actctggtca ctgtctcttc a 351

<210> 344  
<211> 117  
<212> PRT  
<213> Homo sapiens

<400> 344  
Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
5 10 15  
Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr Ser Gly  
20 25 30  
Phe Asp Trp Ser Trp Phe Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
35 40 45  
Met Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Asn Tyr Asn Pro Ser Leu  
50 55 60  
Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe  
65 70 75 80  
Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys  
85 90 95  
Ala Arg Gly Val Ser Ser Leu Ser Ala Tyr Trp Gly Gln Gly Thr Leu  
100 105 110  
Val Thr Val Ser Ser  
115

<210> 345  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 345  
Ser Gly Phe Asp

<210> 346  
<211> 18  
<212> PRT  
<213> Homo sapiens

<400> 346  
Met Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Asn Tyr Asn Pro Ser Leu  
5 10 15  
Lys Ser

<210> 347

eolf-seql.txt

<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 347  
Gly Val Ser Ser Leu Ser Ala Tyr  
5

<210> 348  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 348  
Glu Ile Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
5 10 15  
Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Thr Ile Thr  
20 25 30

<210> 349  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 349  
Trp Ser Trp Phe Arg Lys Phe Pro Gly Asn Lys Met Glu Trp  
5 10

<210> 350  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 350  
Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln  
5 10 15  
Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
20 25 30

<210> 351  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 351  
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 352  
<211> 321  
<212> DNA  
<213> Homo sapiens

<400> 352  
gatgtccaga tgaccagtc tccgtcttat cttgctgcgt ctcttgagaa aagtgtttcc 60  
atcagttgca aggcaagtaa gatcattact aattatcttag cctggatatca acagaaacct 120  
ggggaaccat ataaccttct tatccactct gggtaactt tgcaatctgg cactccatca 180  
aggttcagtg gcagtagatc tggtagagat ttactcttca ccatcagaag cctgcagcct 240

eolf-seql.txt

gaagattttg gactctatta ctgccaacag tattatgaaa acccgtagac gtttggagct 300  
 gggaccaagc tggaactgaa a 321

<210> 353  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 353  
 Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
                     5                    10                    15  
 Glu Ser Val Ser Ile Ser Cys Lys Ala Ser Lys Ile Ile Thr Asn Tyr  
                     20                    25                    30  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Glu Pro Tyr Asn Leu Leu Ile  
                     35                    40                    45  
 His Ser Gly Ser Thr Leu Gln Ser Gly Thr Pro Ser Arg Phe Ser Gly  
                     50                    55                    60  
 Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro  
                     65                    70                    75                    80  
 Glu Asp Phe Gly Leu Tyr Tyr Cys Gln Gln Tyr Tyr Glu Asn Pro Tyr  
                     85                    90                    95  
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
                     100                    105

<210> 354  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 354  
 Lys Ala Ser Lys Ile Ile Thr Asn Tyr Leu Ala  
                     5                    10

<210> 355  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 355  
 Ser Gly Ser Thr Leu Gln Ser  
                     5

<210> 356  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 356  
 Gln Gln Tyr Tyr Glu Asn Pro Tyr Thr  
                     5

<210> 357  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 357  
Asp Val Gln Met Thr Gln Ser Pro Ser Tyr Leu Ala Ala Ser Pro Gly  
5 10 15

Glu Ser Val Ser Ile Ser Cys  
20

<210> 358  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 358  
Trp Tyr Gln Gln Lys Pro Gly Glu Pro Tyr Asn Leu Leu Ile His  
5 10 15

<210> 359  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 359  
Gly Thr Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr  
5 10 15

Leu Thr Ile Arg Ser Leu Gln Pro Glu Asp Phe Gly Leu Tyr Tyr Cys  
20 25 30

<210> 360  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 360  
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
5 10

<210> 361  
<211> 366  
<212> DNA  
<213> Homo sapiens

<400> 361  
caggtgcagc tgaaggagtc aggacctggc ctggtgaagc cctcagagac cctgtctctc 60  
acctgcactg tctctgggtt ctcattaacc agctatcatg tgagctgggt tcgacagcct 120  
ccaggaaagg gtctggaatg gatgggagta atatgggggtg atggaagcac agcatttaat 180  
tcagctctca aatcccgact gagcatcagc agggacacct cgaagagcca agttttctta 240  
aaaatgaaca gtctgcaaac tgaagacaca gccacttact actgtgccag agccgggggtt 300  
tactatgatg gtagttatta ctactttgct tactggggcc aaggcactct ggtcactgtc 360  
tcttca 366

<210> 362  
<211> 122  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 362  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
                   5                  10                  15  
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Tyr  
                   20                  25                  30  
 His Val Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met  
                   35                  40                  45  
 Gly Val Ile Trp Gly Asp Gly Ser Thr Ala Phe Asn Ser Ala Leu Lys  
                   50                  55                  60  
 Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu  
                   65                  70                  75                  80  
 Lys Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala  
                   85                  90                  95  
 Arg Ala Gly Val Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Phe Ala Tyr Trp  
                   100                  105                  110  
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
                   115                  120

<210> 363  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 363  
 Ser Tyr His Val Ser  
                   5

<210> 364  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 364  
 Val Ile Trp Gly Asp Gly Ser Thr Ala Phe Asn Ser Ala Leu Lys Ser  
                   5                  10                  15

<210> 365  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 365  
 Ala Gly Val Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Phe Ala Tyr  
                   5                  10

<210> 366  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 366  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
                   5                  10                  15  
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
                   20                  25                  30

eolf-seql.txt

<210> 367  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 367  
 Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
                     5                                    10

<210> 368  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 368  
 Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu Lys  
                     5                                    10                    15  
 Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
                     20                                    25                    30

<210> 369  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 369  
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
                     5                                    10

<210> 370  
 <211> 321  
 <212> DNA  
 <213> Homo sapiens

<400> 370  
 gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctgggaga aattgtcacc 60  
 atcacatgcc aggcaagcca agacattggg aattgggttg catggtatca gcagaaaccg 120  
 gggaaatctc ctcacctcct gatttatgat gcaaccacct tggcagatgg ggtcccatca 180  
 cggttcagcg gcagtagatc tggcacacag tattctctta agatcagcag actacaagtt 240  
 gaagatattg gaagctatta ctgtcaaaag gctcatagta atccgtggac gttcgggtgga 300  
 ggcaccaagc tggaattgaa a 321

<210> 371  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 371  
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Gly  
                     5                                    10                    15  
 Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp  
                     20                                    25                    30  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro His Leu Leu Ile  
                     35                                    40                    45

eolf-seql.txt

Tyr Asp Ala Thr Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly  
50 55 60  
Ser Arg Ser Gly Thr Gln Tyr Ser Leu Lys Ile Ser Arg Leu Gln Val  
65 70 75 80  
Glu Asp Ile Gly Ser Tyr Tyr Cys Gln Lys Ala His Ser Asn Pro Trp  
85 90 95  
Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
100 105

<210> 372  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 372  
Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala  
5 10

<210> 373  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 373  
Asp Ala Thr Thr Leu Ala Asp  
5

<210> 374  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 374  
Gln Lys Ala His Ser Asn Pro Trp Thr  
5

<210> 375  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 375  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Gly  
5 10 15  
Glu Ile Val Thr Ile Thr Cys  
20

<210> 376  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 376  
Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro His Leu Leu Ile Tyr  
5 10 15

<210> 377  
<211> 32

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 377  
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Tyr Ser  
5 10 15

Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ser Tyr Tyr Cys  
20 25 30

<210> 378  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 378  
Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
5 10

<210> 379  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 379  
gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt cgcagggt 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gcggcactgg 300  
gactggtgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 380  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 380  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg His Trp Asp Trp Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110

eolf-seql.txt

Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 381  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 381  
Ser Tyr Ala Met Ser  
5

<210> 382  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 382  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 383  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 383  
His Trp Asp Trp Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 384  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 384  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 385  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 385  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 386  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 386  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln

eof-seq1.txt

5

10

15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 387  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 387  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 388  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 388  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggccccctc tactgggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 389  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 389  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 390  
<211> 11  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 390  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 391  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 391  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 392  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 392  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 393  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 393  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 394  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 394  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 395  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 395  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 396  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 396  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu

<210> 397  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 397  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
 tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120  
 ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgtgc cagggacatg 300  
 gactactgga gtacttattc gggccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

<210> 398  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 398  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 95  
 Ala Arg Asp Met Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe 110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser 125

<210> 399  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 399  
 Ser Tyr Ala Met Ser 5

<210> 400  
 <211> 17  
 <212> PRT

<213> Homo sapiens

<400> 400

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 401

<211> 16

<212> PRT

<213> Homo sapiens

<400> 401

Asp Met Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 402

<211> 30

<212> PRT

<213> Homo sapiens

<400> 402

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 403

<211> 14

<212> PRT

<213> Homo sapiens

<400> 403

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 404

<211> 32

<212> PRT

<213> Homo sapiens

<400> 404

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 405

<211> 11

<212> PRT

<213> Homo sapiens

<400> 405

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 406

<211> 324

eolf-seql.txt

```

<212>  DNA
<213>  Homo sapiens

<400>  406
tcctatgagc tggctcagcc accctcggtg tcaagtgtccc caggacagac ggccaggatc      60
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc      120
caggcccctc tactgggtgat atataaagac agtgagaggc cctcagggat ccctgagcga      180
ttctctgggt ccggctcagg gacaacagtc acgttgacca tcaaggaggt ccaggcagaa      240
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc      300
ggagggacca aggtcaccgt ccta                                             324

```

```

<210>  407
<211>  108
<212>  PRT
<213>  Homo sapiens

<400>  407
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
           5              10              15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala
           20              25              30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr
           35              40              45

Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
           50              55              60

Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu
           65              70              75              80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr
           85              90              95

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
           100              105

```

```

<210>  408
<211>  11
<212>  PRT
<213>  Homo sapiens

<400>  408
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr
           5              10

```

```

<210>  409
<211>  7
<212>  PRT
<213>  Homo sapiens

```

```

<400>  409
Lys Asp Ser Glu Arg Pro Ser
           5

```

```

<210>  410
<211>  11
<212>  PRT

```

<213> Homo sapiens

<400> 410  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 411  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 411  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Arg Ile Thr Cys  
20

<210> 412  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 412  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 413  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 413  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 414  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 414  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 415  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 415  
gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctatgccca tgagctgggt ccgccaggct 120  
ccaggggaagg ggctggagtg ggtctcagct attagtggtta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cagcgtgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc ccgggaccac 300

eolf-seql.txt

gactactgga gtacttattc ggggtccaact gcttttgcac tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 416  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 416  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp His Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 417  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 417  
Ser Tyr Ala Met Ser  
5

<210> 418  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 418  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 419  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 419  
Asp His Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

eolf-seql.txt

<210> 420  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 420  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 421  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 421  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 422  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 422  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 423  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 423  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 424  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 424  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 425

eolf-seql.txt

<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 425  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 426  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 426  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 427  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 427  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 428  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 428  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 429  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 429  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

eolf-seql.txt

<210> 430  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 430  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   5                  10                  15

<210> 431  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 431  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
                   5                  10                  15  
 Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
                   20                  25                  30

<210> 432  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 432  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 433  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 433  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
 ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaataga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
 gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

<210> 434  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 434  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                   20                  25                  30

eolf-seql.txt

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 435  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 435  
Ser Tyr Ala Met Ser  
5

<210> 436  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 436  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 437  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 437  
Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 438  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 438  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 439  
<211> 14  
<212> PRT

<213> Homo sapiens

<400> 439

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 440

<211> 32

<212> PRT

<213> Homo sapiens

<400> 440

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
20 25 30

<210> 441

<211> 11

<212> PRT

<213> Homo sapiens

<400> 441

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 442

<211> 324

<212> DNA

<213> Homo sapiens

<400> 442

|                                                                    |     |
|--------------------------------------------------------------------|-----|
| tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc  | 60  |
| acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc  | 120 |
| caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga | 180 |
| ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa  | 240 |
| gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc  | 300 |
| ggagggacca aggtcaccgt ccta                                         | 324 |

<210> 443

<211> 108

<212> PRT

<213> Homo sapiens

<400> 443

Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45

Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60

Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
Page 83

65                      70                      75                      80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                             85                      90                      95

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                             100                      105

<210> 444  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 444  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                             5                      10

<210> 445  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 445  
 Lys Asp Ser Glu Arg Pro Ser  
                             5

<210> 446  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 446  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                             5                      10

<210> 447  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 447  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                             5                      10                      15

Thr Ala Arg Ile Thr Cys  
                             20

<210> 448  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 448  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                             5                      10                      15

<210> 449  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 449

eolf-seql.txt

Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 450  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 450  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 451  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 451  
gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaata acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttga gtaaccggcc gtccccacc gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 452  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 452  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Asn Arg Pro Ser Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

eolf-seql.txt

<210> 453  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 453  
 Ser Tyr Ala Met Ser  
 5

<210> 454  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 454  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
 5 10 15

Gly

<210> 455  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 455  
 Asp Arg Asp Phe Trp Ser Asn Arg Pro Ser Pro Thr Ala Phe Asp Leu  
 5 10 15

<210> 456  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 456  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
 20 25 30

<210> 457  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 457  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
 5 10

<210> 458  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 458  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
 20 25 30

eolf-seql.txt

<210> 459  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 459  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                                  10

<210> 460  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 460  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcacctg ccta 324

<210> 461  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 461  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                                  105

<210> 462  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 462  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                                  10

eolf-seql.txt

<210> 463  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 463  
 Lys Asp Ser Glu Arg Pro Ser  
 5

<210> 464  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 464  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
 5 10

<210> 465  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 465  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
 5 10 15

Thr Ala Arg Ile Thr Cys  
 20

<210> 466  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 466  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
 5 10 15

<210> 467  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 467  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
 5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
 20 25 30

<210> 468  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 468  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
 5 10

<210> 469

eolf-seql.txt

<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 469  
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gattttttgga gtggcgcgaa ccggatgacc gctttttgatc tctgggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 470  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 470  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Gly Ala Asn Arg Met Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 471  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 471  
Ser Tyr Ala Met Ser  
5

<210> 472  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 472  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys

5

10

15

Gly

<210> 473  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 473  
 Asp Arg Asp Phe Trp Ser Gly Ala Asn Arg Met Thr Ala Phe Asp Leu  
                   5                                  10                                  15

<210> 474  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 474  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                                  10                                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                                  25                                  30

<210> 475  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 475  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                                  10

<210> 476  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 476  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                                  10                                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
                   20                                  25                                  30

<210> 477  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 477  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                                  10

<210> 478  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 478

| eolf-seq1.txt |            |             |            |            |            |     |
|---------------|------------|-------------|------------|------------|------------|-----|
| tcctatgagc    | tggctcagcc | accctcggtg  | tcagtgtccc | caggacagac | ggccaggatc | 60  |
| acctgctctg    | gagatgcatt | gccaaaggcaa | tatgcttact | ggtaccagca | gaagccaggc | 120 |
| caggcccctc    | tactggtgat | atataaagac  | agtgagaggc | cctcagggat | ccctgagcga | 180 |
| ttctctggct    | ccggctcagg | gacaacagtc  | acgttgacca | tcagtggagt | ccaggcagaa | 240 |
| gacgaggctg    | actattactg | tcaatcagca  | gacagcagtg | gtacctatgt | ggatttcggc | 300 |
| ggagggacca    | aggtcaccgt | ccta        |            |            |            | 324 |

|       |              |
|-------|--------------|
| <210> | 479          |
| <211> | 108          |
| <212> | PRT          |
| <213> | Homo sapiens |

|       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| <400> | 479 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
| Ser   | Tyr | Glu | Leu | Ala | Gln | Pro | Pro | Ser | Val | Ser | Val | Ser | Pro | Gly | Gln |  |
|       |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |  |
| Thr   | Ala | Arg | Ile | Thr | Cys | Ser | Gly | Asp | Ala | Leu | Pro | Arg | Gln | Tyr | Ala |  |
|       |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |  |
| Tyr   | Trp | Tyr | Gln | Gln | Lys | Pro | Gly | Gln | Ala | Pro | Leu | Leu | Val | Ile | Tyr |  |
|       |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |  |
| Lys   | Asp | Ser | Glu | Arg | Pro | Ser | Gly | Ile | Pro | Glu | Arg | Phe | Ser | Gly | Ser |  |
|       | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |
| Gly   | Ser | Gly | Thr | Thr | Val | Thr | Leu | Thr | Ile | Ser | Gly | Val | Gln | Ala | Glu |  |
| 65    |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |
| Asp   | Glu | Ala | Asp | Tyr | Tyr | Cys | Gln | Ser | Ala | Asp | Ser | Ser | Gly | Thr | Tyr |  |
|       |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |
| Val   | Val | Phe | Gly | Gly | Gly | Thr | Lys | Val | Thr | Val | Leu |     |     |     |     |  |
|       |     |     | 100 |     |     |     |     | 105 |     |     |     |     |     |     |     |  |

|       |              |
|-------|--------------|
| <210> | 480          |
| <211> | 11           |
| <212> | PRT          |
| <213> | Homo sapiens |

<400> 480  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

```
<210> 481
<211> 7
<212> PRT
<213> Homo sapiens
```

<400> 481  
Lys Asp Ser Glu Arg Pro Ser  
5

|       |              |
|-------|--------------|
| <210> | 482          |
| <211> | 11           |
| <212> | PRT          |
| <213> | Homo sapiens |

<400> 482  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
Page 91

<210> 483  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 483  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 484  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 484  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 485  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 485  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 486  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 486  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 487  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 487  
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttggg gtggctccag caaggccacg gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

eolf-seql.txt

<210> 488  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 488  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
                   50                  55                  60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
  65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Ala Arg Asp Arg Asp Phe Trp Ser Gly Ser Ser Lys Ala Thr Ala Phe  
                   100                  105                  110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   115                  120                  125

<210> 489  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 489  
 Ser Tyr Ala Met Ser  
                   5

<210> 490  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 490  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
                   5                  10                  15

Gly

<210> 491  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 491  
 Asp Arg Asp Phe Trp Ser Gly Ser Ser Lys Ala Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 492  
 <211> 30

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 492  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 493  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 493  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 494  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 494  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 495  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 495  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 496  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 496  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactgggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 497  
<211> 108  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 497  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 498  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 498  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 499  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 499  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 500  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 500  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                   5                  10

<210> 501  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 501  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys  
                   20

<210> 502  
 <211> 15

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 502  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 503  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 503  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 504  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 504  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 505  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 505  
gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttggg gtcccgggac cggcctcacc gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 506  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 506  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val

eolf-seql.txt

50

55

60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Pro Gly Thr Gly Leu Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 507  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 507  
Ser Tyr Ala Met Ser  
5

<210> 508  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 508  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 509  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 509  
Asp Arg Asp Phe Trp Ser Pro Gly Thr Gly Leu Thr Ala Phe Asp Leu  
5 10 15

<210> 510  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 510  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 511  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 511  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser

<210> 512  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 512  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 513  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 513  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 514  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 514  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggcccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 515  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 515  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95

eolf-seql.txt

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 516  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 516  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 517  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 517  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 518  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 518  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 519  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 519  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Arg Ile Thr Cys  
20

<210> 520  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 520  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 521  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 521  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
Page 99

<210> 522  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 522  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 523  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 523  
 gaggtgcagc tgctggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctttgccca tgagctgggt ccgccaggct 120  
 cctgggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
 gattttttgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cctca 375

<210> 524  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 524  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
                   50                  55                  60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
                   65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
                   100                  105                  110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   115                  120                  125

<210> 525  
 <211> 5  
 <212> PRT

<213> Homo sapiens

<400> 525  
Ser Phe Ala Met Ser  
5

<210> 526  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 526  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 527  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 527  
Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 528  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 528  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 529  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 529  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 530  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 530  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 531  
<211> 11

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 531  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 532  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 532  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 533  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 533  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln 15  
5 10  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala 30  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr 45  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser 60  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu 80  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr 95  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu 105  
100 105

<210> 534  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 534  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr 10  
5 10

<210> 535  
<211> 7  
<212> PRT

<213> Homo sapiens

<400> 535  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 536  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 536  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 537  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 537  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 538  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 538  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 539  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 539  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 540  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 540  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 541  
<211> 375  
<212> DNA  
<213> Homo sapiens

eolf-seql.txt

```
<400> 541
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc      60
tcctgtgcag cctctggatt caccttttagc agctttgccca tgagctgggt cgcagggt      120
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac      180
gcagactccg tgaagggccg gctcaccatc tccagagaca attccaagaa cacgctgtat      240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg      300
gatttttggg gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg      360
gtcaccgtct cgagt                                          375
```

```
<210> 542
<211> 125
<212> PRT
<213> Homo sapiens
```

```
<400> 542
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                    5                      10                      15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
                20                      25                      30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
                35                      40                      45
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
                50                      55                      60
Lys Gly Arg Leu Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
        65                      70                      75                      80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                      90                      95
Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe
                100                      105                      110
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
                115                      120                      125
```

```
<210> 543
<211> 5
<212> PRT
<213> Homo sapiens
```

```
<400> 543
Ser Phe Ala Met Ser
                    5
```

```
<210> 544
<211> 17
<212> PRT
<213> Homo sapiens
```

```
<400> 544
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
                    5                      10                      15
```

Gly

eolf-seql.txt

<210> 545  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 545  
 Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 546  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 546  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 547  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 547  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 548  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 548  
 Arg Leu Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 549  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 549  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 550  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 550  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120

eolf-seql.txt

caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 551  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 551  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 552  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 552  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 553  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 553  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 554  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 554  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                   5                  10

<210> 555

eolf-seql.txt

<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 555  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 556  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 556  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 557  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 557  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 558  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 558  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 559  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 559  
gaggtgcggc tggttgagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctttgcca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtgggtggtag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tctagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gattttttgga gtacttattc ggggtccaact gctttttgatc tctggggcag aggcacctg 360  
gtcaccgtct cgagt 375

<210> 560  
<211> 125

eolf-seql.txt

```

<212>  PRT
<213>  Homo sapiens

<400>  560
Glu Val Arg Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
          5          10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
          20          25          30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
          35          40          45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
          50          55          60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
          65          70          75          80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
          85          90          95

Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe
          100          105          110

Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
          115          120          125

```

```

<210>  561
<211>  5
<212>  PRT
<213>  Homo sapiens

```

```

<400>  561
Ser Phe Ala Met Ser
          5

```

```

<210>  562
<211>  17
<212>  PRT
<213>  Homo sapiens

```

```

<400>  562
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
          5          10          15

```

Gly

```

<210>  563
<211>  16
<212>  PRT
<213>  Homo sapiens

```

```

<400>  563
Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu
          5          10          15

```

```

<210>  564
<211>  30
<212>  PRT
<213>  Homo sapiens

```

```

<400>  564

```

eolf-seql.txt

Glu Val Arg Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 565  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 565  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 566  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 566  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 567  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 567  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 568  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 568  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gtgatgcatt gccaaggcaa tacgcttact ggtaccagca gaagccaggc 120  
caggccctc tactggtgat atataaagac agtgagaggc cctcagggat cccagagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 569  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 569  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

eolf-seql.txt

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
 20 25 30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
 35 40 45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
 50 55 60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
 65 70 75 80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
 85 90 95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
 100 105

<210> 570  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 570  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
 5 10

<210> 571  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 571  
 Lys Asp Ser Glu Arg Pro Ser  
 5

<210> 572  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 572  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
 5 10

<210> 573  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 573  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
 5 10 15

Thr Ala Arg Ile Thr Cys  
 20

<210> 574  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 574

eolf-seql.txt

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 575  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 575  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 576  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 576  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 577  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 577  
gaggtgcagc tgatggagtc tgggggaggc ttggtacagc ctgggggggtc cctgaggctc 60  
tcctgtgcag cctctggatt caccttttagc agctttgcca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
gcagactccg cgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gattttttgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcacctg 360  
gtcaccgtct cctca 375

<210> 578  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 578  
Glu Val Gln Leu Met Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe  
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Ala  
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80

eolf-seql.txt

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110

Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 579  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 579  
Ser Phe Ala Met Ser  
5

<210> 580  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 580  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Ala Lys  
5 10 15

Gly

<210> 581  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 581  
Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 582  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 582  
Glu Val Gln Leu Met Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 583  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 583  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 584

eolf-seql.txt

<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 584  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 585  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 585  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 586  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 586  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggccccctc taccggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 587  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 587  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Pro Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

eolf-seql.txt

<210> 588  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 588  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                                  10

<210> 589  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 589  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 590  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 590  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                   5                                  10

<210> 591  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 591  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                                  10                  15

Thr Ala Arg Ile Thr Cys  
                   20

<210> 592  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 592  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Pro Val Ile Tyr  
                   5                                  10                  15

<210> 593  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 593  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
                   5                                  10                  15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
                   20                                  25                  30

<210> 594

eolf-seql.txt

<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 594  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 595  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 595  
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctggggggcc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctatgccca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcggct attagtggta gtggtggtag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgcgt attactgtgc gagagattgg 300  
gatttttggg gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 596  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 596  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 15  
5 10  
Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 30  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 45  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 60  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 80  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ala Tyr Tyr Cys 95  
85 90 95  
Ala Arg Asp Trp Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe 110  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser 125  
115 120 125

<210> 597  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 597  
Ser Tyr Ala Met Ser

<210> 598  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 598  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
                   5                  10                  15

Gly

<210> 599  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 599  
 Asp Trp Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 600  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 600  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15

Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 601  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 601  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 602  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 602  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ala Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 603  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 603

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 604  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 604  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggcccccc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 605  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 605  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 606  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 606  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 607  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 607  
 Lys Asp Ser Glu Arg Pro Ser

<210> 608  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 608  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                   5                                  10

<210> 609  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 609  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                                  10                                  15

Thr Ala Arg Ile Thr Cys  
                   20

<210> 610  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 610  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   5                                  10                                  15

<210> 611  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 611  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
                   5                                  10                                  15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
                   20                                  25                                  30

<210> 612  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 612  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                                  10

<210> 613  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 613  
 gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctttgcca tgagctgggt ccgccaggct 120

eolf-seql.txt

ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtagtag cacatactac 180  
gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttggg gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 614  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 614  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 615  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 615  
Ser Phe Ala Met Ser  
5

<210> 616  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 616  
Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15  
Gly

<210> 617  
<211> 16

eolf-seql.txt

<212> PRT  
<213> Homo sapiens

<400> 617  
Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 618  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 618  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 619  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 619  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 620  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 620  
Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 621  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 621  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 622  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 622  
tcctatgagc tggcccagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240

## eolf-seql.txt

gacgaggctg actattactg tcaatcagcg gacagcagtg gtacctatgc ggtattcggc 300  
 ggagggacca aggtcacctg ccta 324

<210> 623  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 623  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 624  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 624  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 625  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 625  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 626  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 626  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
                   5                  10

<210> 627  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 627  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys  
                   20

<210> 628  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 628  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   5                  10                  15

<210> 629  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 629  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
                   5                  10                  15  
 Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
                   20                  25                  30

<210> 630  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 630  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 631  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 631  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
 ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
 gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
 gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

<210> 632  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 632

eolf-seql.txt

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 633  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 633  
Ser Tyr Ala Met Ser  
5

<210> 634  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 634  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 635  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 635  
Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 636  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 636  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
Page 124

eolf-seql.txt

35 40 45

Lys Asp Ser Phe Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 642  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 642  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 643  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 643  
Lys Asp Ser Phe Arg Pro Ser  
5

<210> 644  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 644  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
5 10

<210> 645  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 645  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 646  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 646  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

eolf-seql.txt

<210> 647  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 647  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 648  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 648  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 649  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 649  
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 650  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 650  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

eolf-seql.txt

Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110

Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 651  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 651  
Ser Tyr Ala Met Ser  
5

<210> 652  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 652  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 653  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 653  
Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 654  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 654  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 655  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 655  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 656  
<211> 32  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 656  
 Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
                   20                  25                  30

<210> 657  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 657  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 658  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 658  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcacctg ccta 324

<210> 659  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 659  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 660  
 <211> 11  
 <212> PRT

<213> Homo sapiens

<400> 660  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 661  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 661  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 662  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 662  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 663  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 663  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 664  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 664  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 665  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 665  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 666  
<211> 10  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 666  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 667  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 667  
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggaagg ggctggagtg ggtctcagct attagtggta gtgggtggtag cacatactac 180  
gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
gactactgga gtacttattc gggccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 668  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 668  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 15  
5 10  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 30  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 45  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 60  
50 55 60  
Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 80  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 95  
85 90 95  
Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe 110  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser 125  
115 120 125

<210> 669  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 669  
Ser Tyr Ala Met Ser  
5

<210> 670

eolf-seql.txt

<211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 670  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
                   5                  10                  15

Gly

<210> 671  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 671  
 Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 672  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 672  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 673  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 673  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 674  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 674  
 Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
                   20                  25                  30

<210> 675  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 675  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

eolf-seql.txt

<210> 676  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 676  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgc ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 677  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 677  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 678  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 678  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 679  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 679  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 680

eolf-seql.txt

<211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 680  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
                   5                  10

<210> 681  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 681  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys  
                   20

<210> 682  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 682  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   5                  10                  15

<210> 683  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 683  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
                   5                  10                  15  
 Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
                   20                  25                  30

<210> 684  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 684  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 685  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 685  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt ccgccaggct 120  
 ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtagtag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

eolf-seql.txt

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttggga gtacttattc ggggtccaact gcttttgate tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 686  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 686  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 687  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 687  
Ser Tyr Ala Met Ser  
5

<210> 688  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 688  
Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 689  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 689

eolf-seql.txt

Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 690  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 690  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 691  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 691  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 692  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 692  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 693  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 693  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 694  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 694  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

eolf-seql.txt

<210> 695  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 695  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 696  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 696  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 697  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 697  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 698  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 698  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
                   5                  10

<210> 699  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 699  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15

Thr Ala Arg Ile Thr Cys  
20

<210> 700  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 700  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 701  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 701  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 702  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 702  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 703  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 703  
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 704  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 704  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
Page 137

## eolf-seql.txt

20

25

30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
           35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
       50                  55                  60  
 Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
           85                  90                  95  
 Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
          100                 105                 110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
          115                 120                 125

<210> 705  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 705  
 Ser Tyr Ala Met Ser  
           5

<210> 706  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 706  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
           5                  10                 15

Gly

<210> 707  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 707  
 Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
           5                 10                 15

<210> 708  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 708  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
           5                 10                 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
          20                 25                 30

<210> 709

eolf-seql.txt

<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 709  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 710  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 710  
Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 711  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 711  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 712  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 712  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 713  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 713  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60

eolf-seql.txt

Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 714  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 714  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 715  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 715  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 716  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 716  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 717  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 717  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Arg Ile Thr Cys  
20

<210> 718  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 718  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 719  
<211> 32  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 719  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 720  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 720  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 721  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 721  
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gatttttggg gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 722  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 722  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser

115

120

125

<210> 723  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 723  
 Ser Tyr Ala Met Ser  
 5

<210> 724  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 724  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
 5 10 15

Gly

<210> 725  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 725  
 Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
 5 10 15

<210> 726  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 726  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
 20 25 30

<210> 727  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 727  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
 5 10

<210> 728  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 728  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
 5 10 15

eolf-seql.txt

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 729  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 729  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 730  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 730  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgc ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 731  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 731  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln 15  
5 10  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala 30  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr 45  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser 60  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu 80  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr 95  
85 90 95  
Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu 105  
100 105

<210> 732  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 732  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr

5

10

<210> 733  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 733  
 Lys Asp Ser Glu Arg Pro Ser  
 5

<210> 734  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 734  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
 5 10

<210> 735  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 735  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
 5 10 15

Thr Ala Arg Ile Thr Cys  
 20

<210> 736  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 736  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
 5 10 15

<210> 737  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 737  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
 5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
 20 25 30

<210> 738  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 738  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
 5 10

eolf-seql.txt

<210> 739  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 739  
 gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt ccgccaggct 120  
 ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
 gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cagcgtgtat 240  
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
 gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

<210> 740  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 740  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
           50                  55                  60  
 Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
   65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
                   100                  105                  110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
           115                  120                  125

<210> 741  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 741  
 Ser Tyr Ala Met Ser  
                   5

<210> 742  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 742  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 743  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 743  
Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 744  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 744  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 745  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 745  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 746  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 746  
Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
20 25 30

<210> 747  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 747  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 748  
<211> 324  
<212> DNA  
<213> Homo sapiens

eolf-seql.txt

```
<400> 748
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc      60
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc      120
caggccccctc tactggtgat atataaagac agtttcaggc cctcagggat ccctgagcga      180
ttctctgggt cgggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa      240
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc      300
ggagggacca aggtcaccgt ccta                                             324
```

```
<210> 749
<211> 108
<212> PRT
<213> Homo sapiens
```

```
<400> 749
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
                    5                      10                      15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala
                20                      25                      30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr
                35                      40                      45

Lys Asp Ser Phe Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
    50                      55                      60

Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu
    65                      70                      75                      80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr
                85                      90                      95

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
                100                      105
```

```
<210> 750
<211> 11
<212> PRT
<213> Homo sapiens
```

```
<400> 750
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr
                    5                      10
```

```
<210> 751
<211> 7
<212> PRT
<213> Homo sapiens
```

```
<400> 751
Lys Asp Ser Phe Arg Pro Ser
                    5
```

```
<210> 752
<211> 11
<212> PRT
<213> Homo sapiens
```

eolf-seql.txt

<400> 752  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

<210> 753  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 753  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 754  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 754  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 755  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 755  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 756  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 756  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 757  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 757  
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360

gtcaccgtct cgagt

375

<210> 758  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 758  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
                   50                  55                  60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
                   65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
                   100                  105                  110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   115                  120                  125

<210> 759  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 759  
 Ser Tyr Ala Met Ser  
                   5

<210> 760  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 760  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
                   5                  10                  15

Gly

<210> 761  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 761  
 Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

eolf-seql.txt

<210> 762  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 762  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 763  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 763  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 764  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 764  
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
20 25 30

<210> 765  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 765  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 766  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 766  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgc ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 767  
<211> 108  
<212> PRT

<213> Homo sapiens

<400> 767  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
           50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   100                  105

<210> 768  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 768  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
                   5                  10

<210> 769  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 769  
 Lys Asp Ser Glu Arg Pro Ser  
                   5

<210> 770  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 770  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
                   5                  10

<210> 771  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 771  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys  
                   20

eolf-seql.txt

<210> 772  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 772  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 773  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 773  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 774  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 774  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 775  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 775  
gaggtgcagc tggttgagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt caccttttagc agctatgcca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggttag cacatactac 180  
gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
gattttttgga gtacttattc ggggtccaact gctttttgatc tctgggggcag aggaccctg 360  
gtcaccgtct cgagt 375

<210> 776  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 776  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45

eolf-seql.txt

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 777  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 777  
Ser Tyr Ala Met Ser  
5

<210> 778  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 778  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 779  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 779  
Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 780  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 780  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 781  
<211> 14  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 781  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 782  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 782  
Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 783  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 783  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 784  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 784  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggccccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgc ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 785  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 785  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80

eolf-seql.txt

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95

Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 786  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 786  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 787  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 787  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 788  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 788  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
5 10

<210> 789  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 789  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Arg Ile Thr Cys  
20

<210> 790  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 790  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 791  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 791  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

eolf-seql.txt

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
 20 25 30

<210> 792  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 792  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
 5 10

<210> 793  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 793  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt ccgccaggct 120  
 ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
 gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcacctg 360  
 gtcaccgtct cgagt 375

<210> 794  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 794  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 15  
 5 10  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 30  
 20 25 30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 45  
 35 40 45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 60  
 50 55 60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 80  
 65 70 75 80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 95  
 85 90 95  
 Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe 110  
 100 105 110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser 125  
 115 120 125

<210> 795

eolf-seql.txt

<211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 795  
 Ser Tyr Ala Met Ser  
 5

<210> 796  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 796  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
 5 10 15

Gly

<210> 797  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 797  
 Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
 5 10 15

<210> 798  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 798  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
 20 25 30

<210> 799  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 799  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
 5 10

<210> 800  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 800  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
 20 25 30

eolf-seql.txt

<210> 801  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 801  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 802  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 802  
tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactggtgat atataaagac agtttcaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 803  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 803  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Phe Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 804  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 804  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 805

<211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 805  
 Lys Asp Ser Phe Arg Pro Ser  
 5

<210> 806  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 806  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
 5 10

<210> 807  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 807  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
 5 10 15

Thr Ala Arg Ile Thr Cys  
 20

<210> 808  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 808  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
 5 10 15

<210> 809  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 809  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
 5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
 20 25 30

<210> 810  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 810  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
 5 10

<210> 811  
 <211> 375  
 <212> DNA

&lt;213&gt; Homo sapiens

<400> 811  
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctttgcca tgagctgggt ccgccaggct 120  
ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggccacctg 360  
gtcaccgtct cgagt 375

&lt;210&gt; 812

&lt;211&gt; 125

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 812  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60  
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

&lt;210&gt; 813

&lt;211&gt; 5

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 813  
Ser Phe Ala Met Ser  
5

&lt;210&gt; 814

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 814  
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 815  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 815  
 Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 816  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 816  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 817  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 817  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 818  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 818  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
                   20                  25                  30

<210> 819  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 819  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 820  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 820  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc

60

eolf-seql.txt

acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
caggcccctc tactggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
ggagggacca aggtcaccgt ccta 324

<210> 821  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 821  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 822  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 822  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 823  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 823  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 824  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 824  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
5 10

eolf-seql.txt

<210> 825  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 825  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys  
                   20

<210> 826  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 826  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   5                  10                  15

<210> 827  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 827  
 Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
                   5                  10                  15  
 Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
                   20                  25                  30

<210> 828  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 828  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 829  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 829  
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt cacctttagc agctttgcca tgagctgggt ccgccaggct 120  
 ccaggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180  
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
 gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

eolf-seql.txt

<210> 830  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 830  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe  
           20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
           35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val  
           50                  55                  60  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
   65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
           85                  90                  95  
 Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
          100                 105                 110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
       115                 120                 125

<210> 831  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<400> 831  
 Ser Phe Ala Met Ser  
           5

<210> 832  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 832  
 Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
                   5                  10                  15

Gly

<210> 833  
 <211> 16  
 <212> PRT  
 <213> Homo sapiens

<400> 833  
 Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
                   5                  10                  15

<210> 834  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 834  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
                   5                  10                  15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
                   20                  25                  30

<210> 835  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 835  
 Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
                   5                  10

<210> 836  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 836  
 Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
                   20                  25                  30

<210> 837  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 837  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 838  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 838  
 tcctatgagc tggctcagcc accctcggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggcccctc tactggtgat atataaagac agtttcaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgt ggtattcggc 300  
 ggagggacca aggtcaccgt ccta 324

<210> 839  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 839  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln

## eolf-seql.txt

5

10

15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
 20 25 30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
 35 40 45  
 Lys Asp Ser Phe Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
 50 55 60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
 65 70 75 80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
 85 90 95  
 Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
 100 105

<210> 840  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 840  
 Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
 5 10

<210> 841  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 841  
 Lys Asp Ser Phe Arg Pro Ser  
 5

<210> 842  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 842  
 Gln Ser Ala Asp Ser Ser Gly Thr Tyr Val Val  
 5 10

<210> 843  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 843  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
 5 10 15

Thr Ala Arg Ile Thr Cys  
 20

<210> 844  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 844  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 845  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 845  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 846  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 846  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 847  
<211> 375  
<212> DNA  
<213> Homo sapiens

<400> 847  
gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120  
ccaggaagg ggctggagtg ggtctcagct attagtggta gtggtagtag cacatactac 180  
gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
ctgcaaatac acagcctgag agccgaggac acggccgtgt attactgttc gcggcagttc 300  
gactactgga gtacttattc ggggtccaact gcttttgatc tctggggcag aggcaccctg 360  
gtcaccgtct cgagt 375

<210> 848  
<211> 125  
<212> PRT  
<213> Homo sapiens

<400> 848  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val  
50 55 60

eolf-seql.txt

Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ser Arg Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe  
100 105 110  
Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 849  
<211> 5  
<212> PRT  
<213> Homo sapiens

<400> 849  
Ser Tyr Ala Met Ser  
5

<210> 850  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 850  
Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 851  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 851  
Gln Phe Asp Tyr Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 852  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 852  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 853  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 853  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

eolf-seql.txt

<210> 854  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 854  
 Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
                   5                  10                  15  
 Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg  
                   20                  25                  30

<210> 855  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 855  
 Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
                   5                  10

<210> 856  
 <211> 324  
 <212> DNA  
 <213> Homo sapiens

<400> 856  
 tcctatgagc tggctcagcc accctcgggtg tcagtgtccc caggacagac ggccaggatc 60  
 acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
 caggccccctc tactgggtgat atataaagac agtgagaggc cctcagggat ccctgagcga 180  
 ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
 gacgaggctg actattactg tcaatcagca gacagcagtg gtacctatgc ggtattcggc 300  
 ggaggggacca aggtcaccgt ccta 324

<210> 857  
 <211> 108  
 <212> PRT  
 <213> Homo sapiens

<400> 857  
 Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
                   5                  10                  15  
 Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
                   20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
                   35                  40                  45  
 Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
                   50                  55                  60  
 Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
                   65                  70                  75                  80  
 Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
                   85                  90                  95  
 Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu

<210> 858  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 858  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 859  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 859  
Lys Asp Ser Glu Arg Pro Ser  
5

<210> 860  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 860  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
5 10

<210> 861  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 861  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys  
20

<210> 862  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 862  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 863  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 863  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15  
Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

eolf-seql.txt

<210> 864  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 864  
 Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
                   5                  10

<210> 865  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 865  
 gaggtgcagc tggtggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60  
 tcctgtgcag cctctggatt cacctttagc agctttgccca tgagctgggt ccgccaggct 120  
 ccaggggaagg ggctggagtg ggtctcagct attagtggta gtggtagtag cacatactac 180  
 gcagactccg tgaagggccg gttcgccatc tccagagaca attccaagaa cacgctgtat 240  
 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatagg 300  
 gattttttgga gtacttattc ggggtccaact gctttttgatc tctgggggcag aggcaccctg 360  
 gtcaccgtct cgagt 375

<210> 866  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 866  
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 15  
                   5                  10  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe 30  
                   20                  25                  30  
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 45  
                   35                  40                  45  
 Ser Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val 60  
                   50                  55                  60  
 Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 80  
                   65                  70                  75                  80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 95  
                   85                  90                  95  
 Ala Arg Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe 110  
                   100                  105                  110  
 Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser 125  
                   115                  120                  125

<210> 867  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

eolf-seql.txt

<400> 867  
Ser Phe Ala Met Ser  
5

<210> 868  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 868  
Ala Ile Ser Gly Ser Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys  
5 10 15

Gly

<210> 869  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 869  
Asp Arg Asp Phe Trp Ser Thr Tyr Ser Gly Pro Thr Ala Phe Asp Leu  
5 10 15

<210> 870  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 870  
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
20 25 30

<210> 871  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 871  
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser  
5 10

<210> 872  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 872  
Arg Phe Ala Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln  
5 10 15  
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 873  
<211> 11  
<212> PRT  
<213> Homo sapiens

eolf-seql.txt

<400> 873  
Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser  
5 10

<210> 874  
<211> 324  
<212> DNA  
<213> Homo sapiens

<400> 874  
tcctatgagc tggcccagcc accctcgggtg tcagtgtccc caggacagac ggccaggatc 60  
acctgctctg gagatgcatt gccaaggcaa tatgcttact ggtaccagca gaagccaggc 120  
cagggccctc tactggtgat atataaagac agtttcaggc cctcagggat ccctgagcga 180  
ttctctggct ccggctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagaa 240  
gacgaggctg actattactg tcaatcagcg gacagcagtg gtacctatgc ggtattcggc 300  
ggagggacca aggtcacctg ccta 324

<210> 875  
<211> 108  
<212> PRT  
<213> Homo sapiens

<400> 875  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15  
Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
35 40 45  
Lys Asp Ser Phe Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu  
65 70 75 80  
Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Tyr  
85 90 95  
Ala Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
100 105

<210> 876  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 876  
Ser Gly Asp Ala Leu Pro Arg Gln Tyr Ala Tyr  
5 10

<210> 877  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 877  
Lys Asp Ser Phe Arg Pro Ser  
5

<210> 878  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 878  
Gln Ser Ala Asp Ser Ser Gly Thr Tyr Ala Val  
5 10

<210> 879  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 879  
Ser Tyr Glu Leu Ala Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln  
5 10 15

Thr Ala Arg Ile Thr Cys  
20

<210> 880  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 880  
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr  
5 10 15

<210> 881  
<211> 32  
<212> PRT  
<213> Homo sapiens

<400> 881  
Gly Ile Pro Glu Arg Phe Ser Gly Ser Gly Ser Gly Thr Thr Val Thr  
5 10 15

Leu Thr Ile Ser Gly Val Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys  
20 25 30

<210> 882  
<211> 10  
<212> PRT  
<213> Homo sapiens

<400> 882  
Phe Gly Gly Gly Thr Lys Val Thr Val Leu  
5 10

<210> 883  
<211> 366  
<212> DNA  
<213> Rattus rattus

<400> 883  
caggtgcagc tgaaggagtc aggacctggc ctggtgaagc cctcagagac cctgtctctc

eolf-seql.txt

```

acctgcactg tctctgggtt ctcattaacc aactatcatg taaactgggt tcgacagcct      120
ccaggaaagg gtctggagtg gatgggagta atatgggggtg atggaagcac agcatataat      180
tcagctctca aatcccgact gagcatcagc agggacacct cgaagagcca agttttctta      240
aaaatgaaca gtctgcaaac tgaagacaca gccacttact actgtgccag aggcggggat      300
tactatgatg gtagttatta ctacgagggc tactggggcc aaggagtcac ggtcaccgtc      360
tcctca                                          366

```

```

<210>      884
<211>      122
<212>      PRT
<213>      Rattus rattus

```

```

<400>      884
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
              5              10              15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
              20              25              30

His Val Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met
              35              40              45

Gly Val Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys
              50              55              60

Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu
              65              70              75              80

Lys Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
              85              90              95

Arg Gly Gly Asp Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Glu Gly Tyr Trp
              100              105              110

Gly Gln Gly Val Met Val Thr Val Ser Ser
              115              120

```

```

<210>      885
<211>        5
<212>      PRT
<213>      Rattus rattus

```

```

<400>      885
Asn Tyr His Val Asn
              5

```

```

<210>      886
<211>      16
<212>      PRT
<213>      Rattus rattus

```

```

<400>      886
Val Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys Ser
              5              10              15

```

```

<210>      887
<211>      14
<212>      PRT

```

<213> Rattus rattus

<400> 887

Gly Gly Asp Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Glu Gly Tyr  
5 10

<210> 888

<211> 30

<212> PRT

<213> Rattus rattus

<400> 888

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
20 25 30

<210> 889

<211> 14

<212> PRT

<213> Rattus rattus

<400> 889

Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
5 10

<210> 890

<211> 32

<212> PRT

<213> Rattus rattus

<400> 890

Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu Lys  
5 10 15

Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
20 25 30

<210> 891

<211> 11

<212> PRT

<213> Rattus rattus

<400> 891

Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
5 10

<210> 892

<211> 321

<212> DNA

<213> Rattus rattus

<400> 892

gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga aattgtcacc 60

atcacatgcc aggcaagcca ggacattgggt aattggttat catgggtatca gcagaaacca 120

gggaaatctc ctgagctcct gatctatgggt gcaaccagct tggcagatgg ggtcccatca 180

aggttcagcg gcagtagatc tggcacacag ttttctctta agatcagcag actacaggtt 240

gaagatattg gaatctatta ctgtctacag gcttatagtg ctccgtggac gttcgggtgga 300

ggcaccaagc tggaattgaa a

321

<210> 893  
 <211> 107  
 <212> PRT  
 <213> Rattus rattus

<400> 893  
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
                   5                  10                  15  
 Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp  
                   20                  25                  30  
 Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile  
                   35                  40                  45  
 Tyr Gly Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly  
                   50                  55                  60  
 Ser Arg Ser Gly Thr Gln Phe Ser Leu Lys Ile Ser Arg Leu Gln Val  
                   65                  70                  75                  80  
 Glu Asp Ile Gly Ile Tyr Tyr Cys Leu Gln Ala Tyr Ser Ala Pro Trp  
                   85                  90                  95  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
                   100                  105

<210> 894  
 <211> 11  
 <212> PRT  
 <213> Rattus rattus

<400> 894  
 Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ser  
                   5                  10

<210> 895  
 <211> 7  
 <212> PRT  
 <213> Rattus rattus

<400> 895  
 Gly Ala Thr Ser Leu Ala Asp  
                   5

<210> 896  
 <211> 9  
 <212> PRT  
 <213> Rattus rattus

<400> 896  
 Leu Gln Ala Tyr Ser Ala Pro Trp Thr  
                   5

<210> 897  
 <211> 23  
 <212> PRT  
 <213> Rattus rattus

<400> 897

eolf-seql.txt

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15

Glu Ile Val Thr Ile Thr Cys  
20

<210> 898  
<211> 15  
<212> PRT  
<213> Rattus rattus

<400> 898  
Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile Tyr  
5 10 15

<210> 899  
<211> 32  
<212> PRT  
<213> Rattus rattus

<400> 899  
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Phe Ser  
5 10 15

Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ile Tyr Tyr Cys  
20 25 30

<210> 900  
<211> 10  
<212> PRT  
<213> Rattus rattus

<400> 900  
Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
5 10

<210> 901  
<211> 366  
<212> DNA  
<213> Rattus rattus

<400> 901  
cagggtgcagc tgaaggagtc aggacctggc ctggtgaagc cctcagagac cctgtctctc 60  
acctgcactg tctctgggtt ctcatataacc aactatcatg taaactgggt tcgacagcct 120  
ccaggaaagg gtctggagtg gatggggagta atatgggggtg atggaagcac agcatataat 180  
tcagctctca aatccccgact gagcatcagc agggacacct cgaagagcca agttttctta 240  
aaaatgaaca gtctgcaaac tgaagacaca gccacttact actgtgccag aggcggggat 300  
tactatgatg gtagttatta ctacgagggc tactgggggcc aaggagtcac ggtcaccgtc 360  
tcctca 366

<210> 902  
<211> 122  
<212> PRT  
<213> Rattus rattus

<400> 902  
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

## eolf-seql.txt

5 10 15  
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr  
 20 25 30  
 His Val Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met  
 35 40 45  
 Gly Val Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys  
 50 55 60  
 Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu  
 65 70 75 80  
 Lys Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala  
 85 90 95  
 Arg Gly Gly Asp Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Glu Gly Tyr Trp  
 100 105 110  
 Gly Gln Gly Val Met Val Thr Val Ser Ser  
 115 120

<210> 903  
 <211> 5  
 <212> PRT  
 <213> Rattus rattus

<400> 903  
 Asn Tyr His Val Asn  
 5

<210> 904  
 <211> 16  
 <212> PRT  
 <213> Rattus rattus

<400> 904  
 Val Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys Ser  
 5 10 15

<210> 905  
 <211> 14  
 <212> PRT  
 <213> Rattus rattus

<400> 905  
 Gly Gly Asp Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Glu Gly Tyr  
 5 10

<210> 906  
 <211> 30  
 <212> PRT  
 <213> Rattus rattus

<400> 906  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
 20 25 30

<210> 907

eolf-seql.txt

<211> 14  
<212> PRT  
<213> Rattus rattus

<400> 907  
Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
5 10

<210> 908  
<211> 32  
<212> PRT  
<213> Rattus rattus

<400> 908  
Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu Lys  
5 10 15  
Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
20 25 30

<210> 909  
<211> 11  
<212> PRT  
<213> Rattus rattus

<400> 909  
Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
5 10

<210> 910  
<211> 321  
<212> DNA  
<213> Rattus rattus

<400> 910  
gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga aattgtcacc 60  
atcacatgcc aggcaagcca agacattggt aattgggttg catggtatca gcagaaaccg 120  
gggaaatctc ctgagctcct gatttatgat gcaaccagct tggcagatgg ggtcccatca 180  
cggttcagcg gcagtagatc tggcacacag tattctctta agatcagcag actacaggtt 240  
gaagatattg gaagctatta ctgtcaccag gctcatagta atcctcggac gttcgggtgga 300  
ggcaccaagc tggaattgaa a 321

<210> 911  
<211> 107  
<212> PRT  
<213> Rattus rattus

<400> 911  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15  
Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp  
20 25 30  
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile  
35 40 45  
Tyr Asp Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly  
50 55 60

eolf-seql.txt

Ser Arg Ser Gly Thr Gln Tyr Ser Leu Lys Ile Ser Arg Leu Gln Val  
65 70 75 80

Glu Asp Ile Gly Ser Tyr Tyr Cys His Gln Ala His Ser Asn Pro Arg  
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
100 105

<210> 912  
<211> 11  
<212> PRT  
<213> Rattus rattus

<400> 912  
Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala  
5 10

<210> 913  
<211> 7  
<212> PRT  
<213> Rattus rattus

<400> 913  
Asp Ala Thr Ser Leu Ala Asp  
5

<210> 914  
<211> 9  
<212> PRT  
<213> Rattus rattus

<400> 914  
His Gln Ala His Ser Asn Pro Arg Thr  
5

<210> 915  
<211> 23  
<212> PRT  
<213> Rattus rattus

<400> 915  
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
5 10 15

Glu Ile Val Thr Ile Thr Cys  
20

<210> 916  
<211> 15  
<212> PRT  
<213> Rattus rattus

<400> 916  
Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile Tyr  
5 10 15

<210> 917  
<211> 32  
<212> PRT  
<213> Rattus rattus

eolf-seql.txt

<400> 917  
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Tyr Ser  
5 10 15

Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ser Tyr Tyr Cys  
20 25 30

<210> 918  
<211> 10  
<212> PRT  
<213> Rattus rattus

<400> 918  
Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
5 10

<210> 919  
<211> 366  
<212> DNA  
<213> Rattus rattus

<400> 919  
caggtgcagc tgaaggagtc aggacctggc ctggtgaagc cctcagagac cctgtctctc 60  
acctgcactg tctctggggt ctcattaacc aactatcatg taaactgggt tcgacagcct 120  
ccaggaaagg gtctgggagt gatggggagta atatgggggt atggaagcac agcatataat 180  
tcagctctca aatcccgact gagcatcagc agggacacct cgaagagcca agttttctta 240  
aaaatgaaca gtctgcaaac tgaagacaca gccacttact actgtgccag aggcggggat 300  
tactatgatg gtagttatta ctacgagggc tactggggcc aaggagtcac ggtcaccgtc 360  
tcctca 366

<210> 920  
<211> 122  
<212> PRT  
<213> Rattus rattus

<400> 920  
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr  
20 25 30

His Val Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met  
35 40 45

Gly Val Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys  
50 55 60

Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu  
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala  
85 90 95

Arg Gly Gly Asp Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Glu Gly Tyr Trp  
100 105 110

Gly Gln Gly Val Met Val Thr Val Ser Ser

115

120

<210> 921  
 <211> 5  
 <212> PRT  
 <213> Rattus rattus

<400> 921  
 Asn Tyr His Val Asn  
 5

<210> 922  
 <211> 16  
 <212> PRT  
 <213> Rattus rattus

<400> 922  
 Val Ile Trp Gly Asp Gly Ser Thr Ala Tyr Asn Ser Ala Leu Lys Ser  
 5 10 15

<210> 923  
 <211> 14  
 <212> PRT  
 <213> Rattus rattus

<400> 923  
 Gly Gly Asp Tyr Tyr Asp Gly Ser Tyr Tyr Tyr Glu Gly Tyr  
 5 10

<210> 924  
 <211> 30  
 <212> PRT  
 <213> Rattus rattus

<400> 924  
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
 20 25 30

<210> 925  
 <211> 14  
 <212> PRT  
 <213> Rattus rattus

<400> 925  
 Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
 5 10

<210> 926  
 <211> 32  
 <212> PRT  
 <213> Rattus rattus

<400> 926  
 Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Phe Leu Lys  
 5 10 15

Met Asn Ser Leu Gln Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
 20 25 30

eolf-seql.txt

<210> 927  
 <211> 11  
 <212> PRT  
 <213> Rattus rattus

<400> 927  
 Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
                   5                                  10

<210> 928  
 <211> 321  
 <212> DNA  
 <213> Rattus rattus

<400> 928  
 gacatccaga tgacacagtc tcctgcctcc ctgtctgcat ctctggaaga aattgtcacc 60  
 atcacatgcc aggcaagcca agacattggg aattggttgg catggtatca gcagaaaccg 120  
 gggaaatctc ctcaactcct gatttatgat gcaaccagct tggcagatgg ggtcccatca 180  
 cggttcagcg gcagtagatc tggcacacag tattctctta agatcagcag actacaggtt 240  
 gaagatattg gaatctatta ctgtctacag gcttatagtg ctccgtggac gttcgggtgga 300  
 ggcaccaagc tggaattgaa a 321

<210> 929  
 <211> 107  
 <212> PRT  
 <213> Rattus rattus

<400> 929  
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
                   5                                  10                  15  
 Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp  
                   20                                  25                  30  
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile  
                   35                                  40                  45  
 Tyr Asp Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly  
                   50                                  55                  60  
 Ser Arg Ser Gly Thr Gln Tyr Ser Leu Lys Ile Ser Arg Leu Gln Val  
                   65                                  70                  75                  80  
 Glu Asp Ile Gly Ile Tyr Tyr Cys Leu Gln Ala Tyr Ser Ala Pro Trp  
                   85                                  90                  95  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
                   100                                  105

<210> 930  
 <211> 11  
 <212> PRT  
 <213> Rattus rattus

<400> 930  
 Gln Ala Ser Gln Asp Ile Gly Asn Trp Leu Ala  
                   5                                  10

<210> 931  
 <211> 7  
 <212> PRT  
 <213> Rattus rattus

<400> 931  
 Asp Ala Thr Ser Leu Ala Asp  
 5

<210> 932  
 <211> 9  
 <212> PRT  
 <213> Rattus rattus

<400> 932  
 Leu Gln Ala Tyr Ser Ala Pro Trp Thr  
 5

<210> 933  
 <211> 23  
 <212> PRT  
 <213> Rattus rattus

<400> 933  
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu  
 5 10 15  
 Glu Ile Val Thr Ile Thr Cys  
 20

<210> 934  
 <211> 15  
 <212> PRT  
 <213> Rattus rattus

<400> 934  
 Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile Tyr  
 5 10 15

<210> 935  
 <211> 32  
 <212> PRT  
 <213> Rattus rattus

<400> 935  
 Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Gln Tyr Ser  
 5 10 15  
 Leu Lys Ile Ser Arg Leu Gln Val Glu Asp Ile Gly Ile Tyr Tyr Cys  
 20 25 30

<210> 936  
 <211> 10  
 <212> PRT  
 <213> Rattus rattus

<400> 936  
 Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys  
 5 10

<210> 937  
 <211> 360

eolf-seql.txt

<212> DNA  
<213> Mus musculus

<400> 937  
caggtgcagc tgaaggagtc tggacctggc ctggtggcgc cctcacagag cctgtccatc 60  
acttgcaactg tctctggggtt ttcattaacc acctatggta tacactgggt tcgccagcct 120  
ccaggaaagg gtctgggagtg gctgggagta atatggactc gtggaagcac aaattataat 180  
tcggctctca tgtccagact gagcatcagc aaagacaact ccaagagcca agttttctta 240  
aaaatgaaca gtctgcaaac tgatgacaca gccatgtact tctgtgccag agatggttac 300  
tacggttatt actatgcttt ggactactgg ggtcaaggaa cctcagtcac cgtctcctca 360

<210> 938  
<211> 120  
<212> PRT  
<213> Mus musculus

<400> 938  
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln  
5 10 15  
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Thr Tyr  
20 25 30  
Gly Ile His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu  
35 40 45  
Gly Val Ile Trp Thr Arg Gly Ser Thr Asn Tyr Asn Ser Ala Leu Met  
50 55 60  
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu  
65 70 75 80  
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Phe Cys Ala  
85 90 95  
Arg Asp Gly Tyr Tyr Gly Tyr Tyr Tyr Ala Leu Asp Tyr Trp Gly Gln  
100 105 110  
Gly Thr Ser Val Thr Val Ser Ser  
115 120

<210> 939  
<211> 5  
<212> PRT  
<213> Mus musculus

<400> 939  
Thr Tyr Gly Ile His  
5

<210> 940  
<211> 16  
<212> PRT  
<213> Mus musculus

<400> 940  
Val Ile Trp Thr Arg Gly Ser Thr Asn Tyr Asn Ser Ala Leu Met Ser  
5 10 15

eolf-seql.txt

<210> 941  
<211> 12  
<212> PRT  
<213> Mus musculus

<400> 941  
Asp Gly Tyr Tyr Gly Tyr Tyr Tyr Ala Leu Asp Tyr  
5 10

<210> 942  
<211> 30  
<212> PRT  
<213> Mus musculus

<400> 942  
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln  
5 10 15  
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
20 25 30

<210> 943  
<211> 14  
<212> PRT  
<213> Mus musculus

<400> 943  
Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu Gly  
5 10

<210> 944  
<211> 32  
<212> PRT  
<213> Mus musculus

<400> 944  
Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys  
5 10 15  
Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Phe Cys Ala Arg  
20 25 30

<210> 945  
<211> 11  
<212> PRT  
<213> Mus musculus

<400> 945  
Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser  
5 10

<210> 946  
<211> 321  
<212> DNA  
<213> Mus musculus

<400> 946  
caaattgttc tcaaacagtc tccagcaatc atgtctgcat ctccagggga gaaggtcacc 60  
atgacctgca gtgccagctc aagtgttaagt tacatgtact ggtaccagca gaagccagga 120  
tcctcccca gactcctgat ttatgacaca tccaacctgg cttctggagt ccctgttcgc 180

## eolf-seql.txt

ttcagttaca gtgggtctgg gacctcttac tctctcacia tcagccgaat ggaggctgaa 240  
 gatgctgcca cttattactg ccagcagtg agtagttacc cacccatgac gttcgggtgga 300  
 ggcaccaagc tggaatcaa a 321

<210> 947  
 <211> 107  
 <212> PRT  
 <213> Mus musculus

<400> 947  
 Gln Ile Val Leu Lys Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly  
           5                  10                  15  
 Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met  
           20                  25                  30  
 Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Arg Leu Leu Ile Tyr  
           35                  40                  45  
 Asp Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Tyr Ser  
           50                  55                  60  
 Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu  
           65                  70                  75                  80  
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro Pro Met  
           85                  90                  95  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
           100                  105

<210> 948  
 <211> 10  
 <212> PRT  
 <213> Mus musculus

<400> 948  
 Ser Ala Ser Ser Ser Val Ser Tyr Met Tyr  
           5                  10

<210> 949  
 <211> 7  
 <212> PRT  
 <213> Mus musculus

<400> 949  
 Asp Thr Ser Asn Leu Ala Ser  
           5

<210> 950  
 <211> 10  
 <212> PRT  
 <213> Mus musculus

<400> 950  
 Gln Gln Trp Ser Ser Tyr Pro Pro Met Thr  
           5                  10

<210> 951  
 <211> 23  
 <212> PRT

<213> Mus musculus

<400> 951  
Gln Ile Val Leu Lys Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly  
5 10 15

Glu Lys Val Thr Met Thr Cys  
20

<210> 952

<211> 15

<212> PRT

<213> Mus musculus

<400> 952  
Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Arg Leu Leu Ile Tyr  
5 10 15

<210> 953

<211> 32

<212> PRT

<213> Mus musculus

<400> 953  
Gly Val Pro Val Arg Phe Ser Tyr Ser Gly Ser Gly Thr Ser Tyr Ser  
5 10 15

Leu Thr Ile Ser Arg Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys  
20 25 30

<210> 954

<211> 10

<212> PRT

<213> Mus musculus

<400> 954  
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
5 10

<210> 955

<211> 369

<212> DNA

<213> Mus musculus

<400> 955  
cagggtccagc ttcagcagtc tggggctgaa ctggcaaaac ccgggggcctc agtgaggatg 60  
tcctgcaaga cttctggcta caccttttagt acctactgga tgcactgggt aaaacagagg 120  
cctggacagg gtctggaatg gattggatac attaatcctc ccaactggta tactgagtat 180  
aatcagaagt tcaaggacaa ggccacattg actgcagaca aatcctccag cacagcctac 240  
atgcaactga tcagcctgac atctgaagac tctgcagtct attactgtgt gcatgagggg 300  
ggatgatta cgaccgactt tcatgctttg gactactggg gtcaaggaac ctcagtcacc 360  
gtctcctca 369

<210> 956

<211> 123

<212> PRT

<213> Mus musculus

eolf-seql.txt

<400> 956  
 Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala  
                   5                  10                  15  
 Ser Val Arg Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Ser Thr Tyr  
                   20                  25                  30  
 Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
                   35                  40                  45  
 Gly Tyr Ile Asn Pro Pro Thr Gly Tyr Thr Glu Tyr Asn Gln Lys Phe  
                   50                  55                  60  
 Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr  
                   65                  70                  75                  80  
 Met Gln Leu Ile Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
                   85                  90                  95  
 Val His Glu Gly Gly Met Ile Thr Thr Asp Phe His Ala Leu Asp Tyr  
                   100                  105                  110  
 Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser  
                   115                  120

<210> 957  
 <211> 5  
 <212> PRT  
 <213> Mus musculus

<400> 957  
 Thr Tyr Trp Met His  
                   5

<210> 958  
 <211> 17  
 <212> PRT  
 <213> Mus musculus

<400> 958  
 Tyr Ile Asn Pro Pro Thr Gly Tyr Thr Glu Tyr Asn Gln Lys Phe Lys  
                   5                  10                  15

Asp

<210> 959  
 <211> 14  
 <212> PRT  
 <213> Mus musculus

<400> 959  
 Glu Gly Gly Met Ile Thr Thr Asp Phe His Ala Leu Asp Tyr  
                   5                  10

<210> 960  
 <211> 30  
 <212> PRT  
 <213> Mus musculus

<400> 960  
 Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala  
                   5                  10                  15

eolf-seql.txt

Ser Val Arg Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Ser  
20 25 30

<210> 961  
<211> 14  
<212> PRT  
<213> Mus musculus

<400> 961  
Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly  
5 10

<210> 962  
<211> 32  
<212> PRT  
<213> Mus musculus

<400> 962  
Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln  
5 10 15

Leu Ile Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Val His  
20 25 30

<210> 963  
<211> 11  
<212> PRT  
<213> Mus musculus

<400> 963  
Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser  
5 10

<210> 964  
<211> 336  
<212> DNA  
<213> Mus musculus

<400> 964  
gacattgtga tgtcacagtc tccatcctcc ctggctgtgt cagcaggaga gaaggtcact 60  
atgagctgca aatccagtc gagtctgctc aacagtagaa cccgaaagaa ctacttggt 120  
tggtaccagc agaaaccagg gcagtctcct aaactgctga tctactgggc atccactagg 180  
gaatctgggg tccctgatcg cttcacaggc agtggatctg ggacagattt cactctcacc 240  
atcagcagtg tgcaggctga agacctggca gtttattact gcaagcaatc ttataatctg 300  
tacacgttcg gaggggggac caagctggaa ataaaa 336

<210> 965  
<211> 112  
<212> PRT  
<213> Mus musculus

<400> 965  
Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly  
5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser  
20 25 30

eolf-seql.txt

Arg Thr Arg Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln  
35 40 45  
Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val  
50 55 60  
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
65 70 75 80  
Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Lys Gln  
85 90 95  
Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
100 105 110

<210> 966  
<211> 17  
<212> PRT  
<213> Mus musculus

<400> 966  
Lys Ser Ser Gln Ser Leu Leu Asn Ser Arg Thr Arg Lys Asn Tyr Leu  
5 10 15

Ala

<210> 967  
<211> 7  
<212> PRT  
<213> Mus musculus

<400> 967  
Trp Ala Ser Thr Arg Glu Ser  
5

<210> 968  
<211> 8  
<212> PRT  
<213> Mus musculus

<400> 968  
Lys Gln Ser Tyr Asn Leu Tyr Thr  
5

<210> 969  
<211> 23  
<212> PRT  
<213> Mus musculus

<400> 969  
Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly  
5 10 15

Glu Lys Val Thr Met Ser Cys  
20

<210> 970  
<211> 15  
<212> PRT  
<213> Mus musculus

eolf-seql.txt

<400> 970  
Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr  
5 10 15

<210> 971  
<211> 32  
<212> PRT  
<213> Mus musculus

<400> 971  
Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr  
5 10 15  
Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys  
20 25 30

<210> 972  
<211> 10  
<212> PRT  
<213> Mus musculus

<400> 972  
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
5 10

<210> 973  
<211> 360  
<212> DNA  
<213> Mus musculus

<400> 973  
caggtgcagc tgaagcagtc aggacctggc ctagtgcagc cctcacagag cctgtccatc 60  
acctgcacag tctctggttt ctcattaact acctatggtg tacactgggt tcgccagtct 120  
ccaggaaagg gtctggagtg gctgggagtg atatggagtg gtggatccac agactataat 180  
gcagctttca tatccagact gagcatcacc aaggacaatt ccaagagcca agttttcttt 240  
aaaatgaaca gtctgcaagc taatgacaca gccatatatt actgtgccag ggatggttac 300  
tacgcccttt actatgctat ggactactgg ggtcaaggaa cctcagtcac cgtctctctca 360

<210> 974  
<211> 120  
<212> PRT  
<213> Mus musculus

<400> 974  
Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Leu Val Gln Pro Ser Gln  
5 10 15  
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Thr Tyr  
20 25 30  
Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu  
35 40 45  
Gly Val Ile Trp Ser Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Ile  
50 55 60  
Ser Arg Leu Ser Ile Thr Lys Asp Asn Ser Lys Ser Gln Val Phe Phe  
65 70 75 80

eolf-seql.txt

Lys Met Asn Ser Leu Gln Ala Asn Asp Thr Ala Ile Tyr Tyr Cys Ala  
85 90 95

Arg Asp Gly Tyr Tyr Ala Leu Tyr Tyr Ala Met Asp Tyr Trp Gly Gln  
100 105 110

Gly Thr Ser Val Thr Val Ser Ser  
115 120

<210> 975  
<211> 5  
<212> PRT  
<213> Mus musculus

<400> 975  
Thr Tyr Gly Val His  
5

<210> 976  
<211> 16  
<212> PRT  
<213> Mus musculus

<400> 976  
Val Ile Trp Ser Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Ile Ser  
5 10 15

<210> 977  
<211> 12  
<212> PRT  
<213> Mus musculus

<400> 977  
Asp Gly Tyr Tyr Ala Leu Tyr Tyr Ala Met Asp Tyr  
5 10

<210> 978  
<211> 30  
<212> PRT  
<213> Mus musculus

<400> 978  
Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Leu Val Gln Pro Ser Gln  
5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
20 25 30

<210> 979  
<211> 14  
<212> PRT  
<213> Mus musculus

<400> 979  
Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu Gly  
5 10

<210> 980  
<211> 32  
<212> PRT  
<213> Mus musculus

eolf-seql.txt

<400> 980  
 Arg Leu Ser Ile Thr Lys Asp Asn Ser Lys Ser Gln Val Phe Phe Lys  
                   5                  10                  15  
 Met Asn Ser Leu Gln Ala Asn Asp Thr Ala Ile Tyr Tyr Cys Ala Arg  
                   20                  25                  30

<210> 981  
 <211> 11  
 <212> PRT  
 <213> Mus musculus

<400> 981  
 Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser  
                   5                  10

<210> 982  
 <211> 321  
 <212> DNA  
 <213> Mus musculus

<400> 982  
 gacattgtga tgaccagtc tcacaaattc atgtccacat cagtaggaga cagggtcagc 60  
 atcacctgca aggccagtca ggatgtgagt actgctgtag cctgggtatca acagaaacca 120  
 ggacaatctc ctaaactact gatttactcg gcacacctacc ggtacactgg agtcctgat 180  
 cgcttcactg gcagtggatc tgggacggat ttcactttca ccatcagcag tgtgcaggct 240  
 gaagacctgg cagtttatta ctgtcagcaa cattatagta ctccgtggac gttcgggtgga 300  
 ggcaccaagc tggaaatcaa a 321

<210> 983  
 <211> 107  
 <212> PRT  
 <213> Mus musculus

<400> 983  
 Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly  
                   5                  10                  15  
 Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala  
                   20                  25                  30  
 Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile  
                   35                  40                  45  
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly  
                   50                  55                  60  
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala  
                   65                  70                  75                  80  
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp  
                   85                  90                  95  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
                   100                  105

<210> 984  
 <211> 11  
 <212> PRT

<213> Mus musculus

<400> 984  
Lys Ala Ser Gln Asp Val Ser Thr Ala Val Ala  
5 10

<210> 985  
<211> 7  
<212> PRT  
<213> Mus musculus

<400> 985  
Ser Ala Ser Tyr Arg Tyr Thr  
5

<210> 986  
<211> 9  
<212> PRT  
<213> Mus musculus

<400> 986  
Gln Gln His Tyr Ser Thr Pro Trp Thr  
5

<210> 987  
<211> 23  
<212> PRT  
<213> Mus musculus

<400> 987  
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly  
5 10 15

Asp Arg Val Ser Ile Thr Cys  
20

<210> 988  
<211> 15  
<212> PRT  
<213> Mus musculus

<400> 988  
Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr  
5 10 15

<210> 989  
<211> 32  
<212> PRT  
<213> Mus musculus

<400> 989  
Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr  
5 10 15

Phe Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys  
20 25 30

<210> 990  
<211> 10  
<212> PRT  
<213> Mus musculus

eolf-seql.txt

<400> 990  
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
5 10

<210> 991  
<211> 354  
<212> DNA  
<213> Rattus rattus

<400> 991  
caggtgcagc tgaaggagtc aggacctggc ctggtgaagc cctcagagac cctgtctctc 60  
acctgcactg tgtctgggtt ctcattaacc aactatccta taagctgggt tcgacagcct 120  
ccaggaaagg gtctggagtg gatgggagta atatggggtg atggaagcac atcatataat 180  
ttagctctca aatcccgact gagcatcagc agggacacct cgaagagcca agttttatta 240  
aaaatgaaca gtctggaaac tgaagacaca gccacttact actgtgccag agtaggagta 300  
tactacggat tattaggtta ctggggccaa ggagtcatgg tcaccgtctc ctca 354

<210> 992  
<211> 118  
<212> PRT  
<213> Rattus rattus

<400> 992  
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
5 10 15  
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr  
20 25 30  
Pro Ile Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met  
35 40 45  
Gly Val Ile Trp Gly Asp Gly Ser Thr Ser Tyr Asn Leu Ala Leu Lys  
50 55 60  
Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Leu Leu  
65 70 75 80  
Lys Met Asn Ser Leu Glu Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala  
85 90 95  
Arg Val Gly Val Tyr Tyr Gly Leu Leu Gly Tyr Trp Gly Gln Gly Val  
100 105 110  
Met Val Thr Val Ser Ser  
115

<210> 993  
<211> 5  
<212> PRT  
<213> Rattus rattus

<400> 993  
Asn Tyr Pro Ile Ser  
5

<210> 994  
<211> 16  
<212> PRT

<213> Rattus rattus

<400> 994

Val Ile Trp Gly Asp Gly Ser Thr Ser Tyr Asn Leu Ala Leu Lys Ser  
5 10 15

<210> 995

<211> 10

<212> PRT

<213> Rattus rattus

<400> 995

Val Gly Val Tyr Tyr Gly Leu Leu Gly Tyr  
5 10

<210> 996

<211> 30

<212> PRT

<213> Rattus rattus

<400> 996

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr  
20 25 30

<210> 997

<211> 14

<212> PRT

<213> Rattus rattus

<400> 997

Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Met Gly  
5 10

<210> 998

<211> 32

<212> PRT

<213> Rattus rattus

<400> 998

Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Ser Gln Val Leu Leu Lys  
5 10 15

Met Asn Ser Leu Glu Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg  
20 25 30

<210> 999

<211> 11

<212> PRT

<213> Rattus rattus

<400> 999

Trp Gly Gln Gly Val Met Val Thr Val Ser Ser  
5 10

<210> 1000

<211> 321

<212> DNA

<213> Rattus rattus

eolf-seql.txt

<400> 1000  
aacactgtga tgactcagtc tcccacatcc atgttcagat cagtaggaga cagggtcacc 60  
atgaactgca aggccagtca gaatgtgggt actaatgtag actggtacca acagaaaaca 120  
gggcagtctc ctaaactgct tatctatggg gcatccaacc ggtacactgg agtccctgat 180  
cgcttcacag gcagtggatc tggaacagat ttcactctca ccatcagcaa catgcaggct 240  
gaagacttgg ctgtttatta ctgtttacag tataactaca atccgtacac gtttggagct 300  
gggaccaagc tggaactgaa a 321

<210> 1001  
<211> 107  
<212> PRT  
<213> Rattus rattus

<400> 1001  
Asn Thr Val Met Thr Gln Ser Pro Thr Ser Met Phe Arg Ser Val Gly  
5 10 15  
Asp Arg Val Thr Met Asn Cys Lys Ala Ser Gln Asn Val Gly Thr Asn  
20 25 30  
Val Asp Trp Tyr Gln Gln Lys Thr Gly Gln Ser Pro Lys Leu Leu Ile  
35 40 45  
Tyr Gly Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly  
50 55 60  
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Met Gln Ala  
65 70 75 80  
Glu Asp Leu Ala Val Tyr Tyr Cys Leu Gln Tyr Asn Tyr Asn Pro Tyr  
85 90 95  
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
100 105

<210> 1002  
<211> 11  
<212> PRT  
<213> Rattus rattus

<400> 1002  
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Asp  
5 10

<210> 1003  
<211> 7  
<212> PRT  
<213> Rattus rattus

<400> 1003  
Gly Ala Ser Asn Arg Tyr Thr  
5

<210> 1004  
<211> 9  
<212> PRT  
<213> Rattus rattus

<400> 1004

Leu Gln Tyr Asn Tyr Asn Pro Tyr Thr  
5

<210> 1005  
<211> 23  
<212> PRT  
<213> Rattus rattus

<400> 1005  
Asn Thr Val Met Thr Gln Ser Pro Thr Ser Met Phe Arg Ser Val Gly  
5 10 15

Asp Arg Val Thr Met Asn Cys  
20

<210> 1006  
<211> 15  
<212> PRT  
<213> Rattus rattus

<400> 16  
Trp Tyr Gln Gln Lys Thr Gly Gln Ser Pro Lys Leu Leu Ile Tyr  
5 10 15

<210> 1007  
<211> 32  
<212> PRT  
<213> Rattus rattus

<400> 1007  
Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr  
5 10 15

Leu Thr Ile Ser Asn Met Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys  
20 25 30

<210> 1008  
<211> 10  
<212> PRT  
<213> Rattus rattus

<400> 1008  
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
5 10