CLAIMS

1. Use of a T cell activating agent and an immune checkpoint inhibitor in the manufacture of a medicament for increasing nucleic acid damage of a hyperproliferating cell or for the prophylaxis or treatment of a cell proliferative disorder in a mammal.

2. Use of a:

T cell activating agent and/or an immune checkpoint inhibitor; and

a peptide compound, wherein the peptide compound comprises any of the following sequences:

A) a peptide comprising residues denoted P1-P6, with the structure, P1, P2, P3, P4, P5, P6 or P6, P5, P4, P3, P2, P1;

wherein P1 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), an amino acid that occupies a similar side chain space, or any amino acid with one or two aromatic, piperidine, pyrazine, pyrimidine, piperazine, morpholine or pyrimidine group(s), or one indole, pentalene, indene, naphthalene, benzofuran, benzothiophene, quinoline, indoline, chroman, quinoxaline, quinazoline group in the side chain;

wherein P2 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, an amino acid that occupies a similar side chain space, or any amino acid with one or two aromatic, piperidine, pyrazine, pyrimidine, piperazine, morpholine or pyrimidine group(s), or one indole, pentalene, indene, naphthalene, benzofuran, benzothiophene, quinoline, indoline, chroman, quinoxaline, or quinazoline group in the side chain;

wherein P3, P4, P5 are any amino acid, or wherein one or more of P3, P4, P5 is a simple carbon chain such that the distance between P2 and P6 is about the same as the distance when each of P3, P4, P5 are amino acids;

wherein P6 is Bpa, Phe4NO2, any one amino acid and Tyr, any one amino acid and Phe, any amino acid, or nothing; or

B) the peptide of A), wherein the amino acid having a simple carbon chain is

11-aminoundecanoic acid, 10-aminodecanoic acid, 9-aminononanoic acid, 8-aminocaprylic acid, 7-aminoheptanoic acid, 6-aminocaproic acid, or a similar structure with one or more unsaturated carbon bonds, and/or

wherein the any one amino acid is Ser, and/or

wherein P4 is Trp, and/or

wherein the amino acid that occupies a similar side chain space is Tyr or Phe; or

C) a peptide comprising residues denoted P1-P12, with any the following structures:

P1, P2, P3, P4, P5, P6 ; P6, P5, P4, P3, P2, P1; P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12; P1, P2, P3, P4, P5, P6, P12, P11, P10, P9, P8, P7; P6, P5, P4, P3, P2, P1, P7, P8, P9, P10, P11, P12; P6, P5, P4, P3, P2, P1, P12, P11, P10, P9, P8, P7; P7, P8, P9, P10, P11, P12, P1, P2, P3, P4, P5, P6; P7, P8, P9, P10, P11, P12, P6, P5, P4, P3, P2, P1; P12, P11, P10, P9, P8, P7, P1, P2, P3, P4, P5, P6; P12, P11, P10, P9, P8, P7, P6, P5, P4, P3, P2, P1; P12, P11, P6, P9, P8, P7, P2, P1; P12, P11, P10, P6, P9, P4, P7, P2, P1; P1, P2, P7, P8, P9, P6, P11, P12; or P1, P2, P7, P4, P9, P6, P10, P11, P12;

wherein P1 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, an amino acid that occupies a similar side chain space (e.g. d- or l-Tyr, d- or l-Phe), or any amino acid with one or two aromatic, piperidine, pyrazine, pyrimidine, piperazine, morpholine or pyrimidine group(s), or one indole, pentalene, indene, naphthalene, benzofuran, benzothiophene, quinoline, indoline, chroman, quinoxaline, or quinazoline group in the side chain;

wherein P2 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), or an amino acid that occupies a similar side chain space, or any amino acid with one or two aromatic, piperidine, pyrazine, pyrimidine, piperazine, morpholine or pyrimidine group(s), or one indole, pentalene, indene, naphthalene, benzofuran, benzothiophene, quinoline, indoline, chroman, quinoxaline, quinazoline group in the side chain;

wherein P3, P4, P5 are any amino acid, or wherein one or more of P3, P4, P5 is a simple carbon chain such that the distance between P2 and P6 is about the same as the distance when each of P3, P4, P5 are amino acids;

wherein P6 is Bpa, Phe4NO2, any one amino acid and Tyr, any one amino acid and Phe; and

wherein at least three of P7, P8, P9, P10, P11, P12 are basic amino acids with the rest being any amino acid or absent; or

D) the peptide of C), wherein the amino acid having a simple carbon chain is 11-aminoundecanoic acid, 10-aminodecanoic acid, 9-aminononanoic acid, 8-aminocaprylic acid, 7-aminoheptanoic acid, 6-aminocaproic acid, or a similar structure with one or more unsaturated carbon bonds, and/or,

wherein the any one amino acid is Ser, and/or,

wherein P4 is Trp, and/or,

wherein the amino acid that occupies a similar side chain space is Tyr or Phe; or

E) a peptide comprising residues denoted P1-P12, with any the following structures:
P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12; P12, P11, P10, P9, P8, P7, P6, P5, P4, P3, P2, P1; P12, P11, P10, P6, P9, P4, P7, P2, P1; or P1, P2, P7, P4, P9, P6, P10, P11, P12;

wherein P1 isCha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, an amino acid that occupies a similar side chain space, or any amino acid with one or two aromatic, piperidine, pyrazine, pyrimidine, piperazine, morpholine or pyrimidine group(s), or one indole, pentalene, indene, naphthalene, benzofuran, benzothiophene, quinoline, indoline, chroman, quinoxaline, or quinazoline group in the side chain;

wherein P2 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), an amino acid that occupies a similar side chain space, or any amino acid with one or two aromatic, piperidine, pyrazine, pyrimidine, piperazine, morpholine or pyrimidine group(s), or one indole, pentalene, indene, naphthalene, benzofuran, benzothiophene, quinoline, indoline, chroman, quinoxaline, quinazoline group in the side chain;

wherein P3, P4, P5 are any amino acid, or wherein one or more of P3, P4, P5 is a simple carbon chain such that the distance between P2 and P6 is about the same as the distance when each of P3, P4, P5 are amino acids;

wherein P6 is Bpa, Phe4NO2, any one amino acid and Tyr, any one amino acid and Phe, any amino acid, or nothing; and

wherein at least three of P7, P8, P9, P10, P11, P12 are basic amino acids with the rest being any amino acid or absent; or

F) the peptide of E), wherein the amino acid having a simple carbon chain is aminoundecanoic acid or 8-aminocaprylic acid, and/or,

wherein the any one amino acid is Ser, and/or,

wherein the amino acid that occupies a similar side chain space is Tyr or Phe; or

G) a peptide comprising residues denoted P1-P12, with any the following structures: P1, P2, P3, P4, P5, P6 or P6, P5, P4, P3, P2, P1,

wherein P1 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, Tyr, or Phe;

wherein P2 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, Tyr, or Phe;

wherein P3 is Ser, Arg, Cys, Pro, or Asn;

wherein P4 is Trp;

wherein P5 is Ser, Arg, or Asn; or

wherein P3, P4, P5 is a single aminoundecanoic acid or a single 8-aminocaprylic acid; and

wherein P6 is Bpa, Phe4NO2, (Ser-Tyr), or (Ser-Phe); or

H) a peptide comprising residues denoted P1-P12, with any the following structures:

P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12; P1, P2, P3, P4, P5, P6, P12, P11, P10, P9, P8, P7; P6, P5, P4, P3, P2, P1, P7, P8, P9, P10, P11, P12; P6, P5, P4, P3, P2, P1, P12, P11, P10, P9, P8, P7; P7, P8, P9, P10, P11, P12, P1, P2, P3, P4, P5, P6; P7, P8, P9, P10, P11, P12, P6, P5, P4, P3, P2, P1; P12, P11, P10, P9, P8, P7, P1, P2, P3, P4, P5, P6; P12, P11, P10, P9, P8, P7, P6, P5, P4, P3, P2, P1; P12, P11, P6, P9, P8, P7, P2, P1; P12, P11, P10, P6, P9, P4, P7, P2, P1; P1, P2, P7, P8, P9, P6, P11, P12; or P1, P2, P7, P4, P9, P6, P10, P11, P12;

wherein P1 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, Tyr, or Phe;

wherein P2 is Cha, Nal(2), (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3), Bpa, Phe4NO2, Tyr, or Phe;

wherein P3 is Ser, Arg, Cys, Pro, or Asn;

wherein P4 is Trp;

wherein P5 is Ser, Arg, or Asn; or

wherein P3, P4, P5 is a single aminoundecanoic acid or a single 8-aminocaprylic acid;

wherein P6 is Bpa, Phe4NO2, (d-Ser-d-Tyr), or (d-Ser-d-Phe); and

wherein at least three of P7, P8, P9, P10, P11, P12 are Arg or Lys with the rest being any amino acid or absent; or

I) a peptide comprising residues denoted P1-P12, with any the following structures:

P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12; P12, P11, P10, P9, P8, P7, P6, P5, P4, P3, P2, P1; P12, P11, P10, P6, P9, P4, P7, P2, P1; or P1, P2, P7, P4, P9, P6, P10, P11, P12;

wherein P1 is Cha, or Nal(2);

wherein P2 is (Phe-2,3,4,5,6-F), (Phe-3,4,5F), (Phe-4CF3);

wherein P3 is Ser;

wherein P4 is Trp;

wherein P5 is Ser or Asn;

wherein P6 is Bpa, Phe4NO2, (Ser-Tyr), or (Ser-Phe); and

wherein at least three of P7, P8, P9, P10, P11, P12 are Arg with the rest being any amino acid or absent; or

J) a peptide comprising residues denoted P1-P12, with any the following structures: P1, P2, P3, P4, P5, P6 or P6, P5, P4, P3, P2, P1;

wherein P1 is Cha, or Nal(2);

wherein P2 is (Phe-2,3,4,5,6-F), (Phe-3,4,5F) or (Phe-4CF3);

wherein P3 is Ser;

wherein P4 is Trp;

wherein P5 is Ser; and

wherein P6 is Bpa, or (Ser-Tyr); or

K) a peptide comprising residues denoted P1-P12, with any the following structures:

P1, P2, P3, P4, P5, P6; P6, P5, P4, P3, P2, P1; P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12; P1, P2, P3, P4, P5, P6, P12, P11, P10, P9, P8, P7; P6, P5, P4, P3, P2, P1, P7, P8, P9, P10, P11, P12; P6, P5, P4, P3, P2, P1, P12, P11, P10, P9, P8, P7; P7, P8, P9, P10, P11, P12, P1, P2, P3, P4, P5, P6; P7, P8, P9, P10, P11, P12, P6, P5, P4, P3, P2, P1; P12, P11, P10, P9, P8, P7, P1, P2, P3, P4, P5, P6; P12, P11, P10, P9, P8, P7, P6, P5, P4, P3, P2, P1; P12, P11, P6, P9, P8, P7, P2, P1; P12, P11, P10, P6, P9, P4, P7, P2, P1; P1, P2, P7, P8, P9, P6, P11, P12; or P1, P2, P7, P4, P9, P6, P10, P11, P12;

wherein P1 is Cha, orNal(2);

wherein P2 is (Phe-2,3,4,5,6-F), (Phe-3,4,5F) or (Phe-4CF3);

wherein P3 is any amino acid;

wherein P4 is d- or l-Trp;

wherein P5 is any amino acid;

wherein P6 is Bpa or (Ser-Tyr);

wherein P7 is Arg;

wherein P8 is Arg;

wherein P9 is Arg;

wherein P10 is Gln or Arg;

wherein P11 is Arg; and

wherein P12 is d- or l-Arg, or

L) the peptide of K), wherein the any amino acid is Ser, or Pro; or

M) a peptide comprising residues denoted P1-P12, with any the following structures:

P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12; P12, P11, P10, P9, P8, P7, P6, P5, P4, P3, P2, P1; P12, P11, P10, P6, P9, P4, P7, P2, P1; or P1, P2, P7, P4, P9, P6, P10, P11, P12;

wherein P1 is Cha or Nal(2);

wherein P2 is (Phe-2,3,4,5,6-F);

wherein P3 is Ser;

wherein P4 is Trp;

wherein P5 is Ser;

wherein P6 is Bpa or (Ser-Tyr);

wherein P7 is Arg;

wherein P8 is Arg;

wherein P9 is Arg;

wherein P10 is Gln or Arg;

wherein P11 is Arg; and

wherein P12 is Arg; or

a prodrug thereof or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for increasing nucleic acid damage of a hyperproliferating cell or for the prophylaxis or treatment of a cell proliferative disorder in a mammal.

3. The use of claim 2, wherein the peptide compound comprises any the following sequences: (d-Bpa) (d-Ser)(d-Trp)(d-Ser) (d-Phe-2,3,4,5,6-F)(d-Cha)(d-Arg) (d-Arg) (d-Arg) (d-Gln)(d-Arg) (d-Arg); (d-Arg) (d-Arg) (d-Arg) (d-Gln)(d-Arg) (d-Arg) (d-Bpa)(d-Ser)(d-Trp)(d-Ser)(d-Phe-2,3,4,5,6-F) (d-Cha); (d-Bpa) (d-Ser)(d-Trp)(d-Ser) (d-Phe-2,3,4,5,6-F)(d-Cha)(d-Arg) (d-Arg) (d-Gln) (d-Arg) (d-Arg) (d-Arg) (SEQ ID NO:59); (d-Arg) (d-Arg) (d-Gln) (d-Arg) (d-Arg) (d-Arg) (d-Bpa) (d-Ser)(d-Trp)(d-Ser) (d-Phe-2,3,4,5,6-F) (d-Cha); (d-Cha) (d-Phe-2,3,4,5,6-F) (d-Ser)(d-Trp)(d-Ser) (d-Bpa) (d-Arg) (d-Arg) (d-Arg) (d-Gln)(d-Arg) (d-Arg); (d-Arg) (d-Arg) (d-Arg) (d-Gln)

(d-Arg)(d-Arg)(d-Cha)(d-Phe-2,3,4,5,6-F)(d-Ser)(d-Trp)(d-Ser)(d-Bpa);

(d-Cha)(d-Phe-2,3,4,5,6-F)(d-Ser)(d-Trp)(d-Ser)(d-Bpa)(d-Arg)(d-Arg) (d-Gln) (d-Arg) (d-Arg) (d-Arg); (d-Arg) (d-Arg) (d-Gln) (d-Arg) (d-Arg) (d-Arg) (d-Cha)

(d-Phe-2,3,4,5,6-F) (d-Ser)(d-Trp)(d-Ser) (d-Bpa) (SEQ ID NO:64); (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Cha) (d-Phe-2,3,4,5,6-F) (d-Ser) (d-Trp)(d-Ser)(d-Bpa); (d-Cha)(d-Phe-2,3,4,5,6-F) (d-Ser) (d-Trp)(d-Ser)(d-Bpa)(d-Arg)(d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg); (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Bpa) (d-Ser)(d-Trp)(d-Ser) (d-Phe-2,3,4,5,6-F)(d-Cha); (d-Bpa) (d-Ser) (d-Trp)(d-Ser) (d-Phe-2,3,4,5,6-F)(d-Cha) (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg) (d-Arg); (d-Arg)(d-Arg)(d-Bpa) (d-Arg) (d-Arg) (d-Arg) (d-Phe-2,3,4,5,6-F)(d-Cha) (SEQ ID NO:69); (d-Cha) (d-Phe-2,3,4,5,6-F) (d-Arg) (d-Arg) (d-Arg) (d-Bpa) (d-Arg)(d-Arg); (d-Arg) (d-Arg) (d-Arg) (d-Bpa) (d-Arg)(d-Trp) (d-Arg) (d-Phe-2,3,4,5,6-F)(d-Cha); (d-Cha) (d-Phe-2,3,4,5,6-F) (d-Arg)(d-Trp) (d-Arg) (d-Bpa) (d-Arg) (d-Arg) (d-Arg); (d-Arg)(d-Arg)(d-Arg)(d-Arg)(d-Bpa) (d-Arg)(d-Trp)(d-Arg) (d-Phe-2,3,4,5,6-F) (d-Cha); (d-Cha) (d-Phe-2,3,4,5,6-F) (d-Arg) (d-Trp)(d-Arg) (d-Bpa) (d-Arg) (d-Arg) (d-Arg) (d-Arg); (d-Arg) (d-Arg)(d-Arg)(d-Bpa)(d-Arg)(d-Arg) (d-Arg) (d-Phe-2,3,4,5,6-F)(d-Cha); or (d-Cha) (d-Phe-2,3,4,5,6-F) (d-Arg) (d-Arg) (d-Arg) (d-Bpa) (d-Arg) (d-Arg) (d-Arg).

4. The use of claim 2, wherein the peptide compound comprises: (d-Bpa)(d-Ser)(d-Trp)(d-Ser)(d-Phe-2,3,4,5,6-F)(d-Cha) (SEQ ID NO:1).

5. The use of any of claims 1-3, wherein the T cell activating agent targets CD28, OX40, GITR, CD137, CD27, or HVEM.

6. The use of any of claims 1-4, wherein the T cell activating agent comprises an anti-CD28, anti-OX40, anti-GITR, anti-CD137, anti-CD27, or anti-HVEM antibody.

7. The use of any of claims 1-4, wherein the immune checkpoint inhibitor targets CTLA-4, PD1, PD-L1, PDL2, VISTA, TIM3, LAG-3 or BTLA.

8. The use of any of claims 1-4, wherein the immune checkpoint inhibitor comprises an anti-CTLA-4, anti-PD1, anti-PD-L1, anti-PDL2, anti-VISTA, anti-TIM3, anti-LAG-3 or anti-BTLA antibody.

9. The use of claims 6 or 8, wherein the antibody comprises a subsequence that binds to CD28, OX40, GITR, CD137, CD27, HVEM, CTLA-4, PD1, PD-L1, PDL2, VISTA, TIM3, LAG-3 or BTLA.

10. The use of claims 6 or 8, wherein the antibody comprises a bi-specific antibody that binds to one or more of CD28, OX40, GITR, CD137, CD27, HVEM, CTLA-4, PD1, PD-L1, PDL2, VISTA, TIM3, LAG-3 and BTLA.

11. The use of claims 6, 8 or 9, wherein the antibody or subsequence comprises a mammalian antibody.

12. The use of claims 6, 8 or 9, wherein the antibody or subsequence comprises a human, humanized, primatized or chimeric antibody that binds to CD28, OX40, GITR, CD137, CD27, HVEM, CTLA-4, PD1, PD-L1, PDL2, VISTA, TIM3, LAG-3 or BTLA.

13. The use of claims 6, 8 or 9, wherein the antibody or subsequence comprises an Fab, Fab', $F(ab')_2$, Fv, Fd, single-chain Fv (scFv), disulfide-linked Fvs (sdFv), V_L, V_H, Camel Ig, V-NAR, VHH, trispecific (Fab_3), bispecific (Fab_2), diabody ($(V_L\text{-}V_H)_2$ or $(V_H\text{-}V_L)_2$), triabody (trivalent), tetrabody (tetravalent), minibody ($(scFv\text{-}C_H3)_2$), bispecific single-chain Fv (Bis-scFv), IgGdeltaCH2, scFv-Fc, $(scFv)_2$-Fc, affibody, aptamer, avimer or nanobody.

14. The use of any of claims 1-13, wherein the mammal has a white blood cell count within a normal range

15. The use of any of claims 1-13, wherein the mammal has a white blood cell count of less than about 11,000 white blood cells per microliter (wbc/µl) of blood.

16. The use of any of claims 1-13, wherein the mammal has a white blood cell count between about 4,000 to about 11,000 white blood cells per microliter (wbc/µl) of blood.

17. The use of any of claims 1-13, wherein the mammal has a white blood cell count of less than about 10,000 white blood cells per microliter (wbc/µl) of blood.

18. The use of any of claims 1-13, wherein the mammal has a white blood cell count of less than about 9,000 white blood cells per microliter (wbc/µl) of blood.

19. The use of any of claims 1-13, wherein the mammal has a white blood cell count between about 4,000 to about 9,000 white blood cells per microliter (wbc/µl) of blood.

20. The use of any of claims 1-13, wherein the mammal has a white blood cell count of less than about 8,000 white blood cells per microliter (wbc/µl) of blood.

21. The use of any of claims 1-13, wherein the mammal has a white blood cell count of less than about 7,000 white blood cells per microliter (wbc/µl) of blood.

22. The use of any of claims 1-13, wherein the mammal has a white blood cell count of less than upper normal limit by each clinical laboratories white blood cells per microliter (wbc/µl) of blood.

23. The use of any of claims 1-13, wherein the peptide compound, T cell activating agent and/or immune checkpoint inhibitor comprises a pharmaceutical formulation.

24. The use of any of claims 2-13, wherein the pharmaceutically acceptable salt thereof is selected from acetate, sulfonate, sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, phosphate, monohydrogen-phosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, propionate, decanoate, caprylate, acrylate,

formate, isobutyrate, caproate, heptanoate, propiolate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, butyne-1,4-dioate, hexyne-1,6-dioate, benzoate, chlorobenzoate, methyl benzoates, dinitrobenzoates, hydroxybenzoates, methoxybenzoates, phthalates, , xylenesulfonate, phenylacetate, phenylpropionate, phenylbutyrate, citrate, lactate, γ-hydroxybutyrate, glycolate, tartrate, methane-sulfonate, propanesulfonate, naphthalene-1-sulfonate, naphthalene-2-sulfonate, and mandelate.

25. The use of any of claims 2-13, wherein the peptide compound has a length from 6 to 10, 10 to 15, 15 to 20, 20 to 25, 25 to 30, 30 to 40, 40 to 50, 50 to 75, 75 to 100, 100 to 150, 150 to 200, or 200 to 300 amino acid residues.

26. The use of any of claims 2-13, wherein the peptide compound further comprises a cell penetrating molecule attached or conjugated thereto.

27. The of claim 26, wherein the cell penetrating molecule is joined to the peptide compound by a covalent bond, or a peptide or a non-peptide linker.

28. The use of claim 26, wherein the cell penetrating peptide comprises an alternating pattern of polar/charged amino acids and non-polar, hydrophobic amino acids.

29. The use of claim 26, wherein the cell penetrating peptide comprises a polycationic or amphipathic alpha-helix structure.

30. The use of claims 2 or 26, wherein the peptide compound and/or the cell penetrating peptide comprises L- or D-isomer amino acids, or a mixture of L- and D-isomer amino acids.

31. The use of claim 26, wherein the cell penetrating peptide comprises a poly-Arginine (Arg) sequence.

32. The use of claim 26, wherein the cell penetrating peptide comprises or consists of (d-Arg)(d-Arg)(d-Arg)(d-Gln)(d-Arg)(d-Arg).

33. The use of any of claims 2-13, wherein the peptide compound is to be administered prior to, with or after the T cell activating agent and/or immune checkpoint inhibitor.

34. The use of any of claims 2-13, wherein the peptide compound is to be administered as a combination with the T cell activating agent and/or immune checkpoint inhibitor.

35. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 48 hours prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

36. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 24 hours prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

37. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 12 hours prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

38. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 6 hours prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

39. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 4 hours prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

40. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 2 hours prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

41. The use of any of claims 2-13, wherein the peptide compound is to be administered less than 1 hour prior to or after the T cell activating agent and/or immune checkpoint inhibitor is to be administered.

42. The use of any of claims 1-13, wherein the medicament further comprises a nucleic acid damaging agent, a nucleic acid damaging treatment, an anti-proliferative agent, or an anti-proliferative treatment.

43. The use of claim 42, wherein the nucleic acid damaging agent, nucleic acid damaging treatment, anti-proliferative agent, or anti-proliferative treatment comprises surgical resection, radiotherapy, ionizing or chemical radiation therapy, chemotherapy, immunotherapy, local or regional thermal (hyperthermia) therapy, vaccination, an alkylating agent, an anti-metabolite, a plant extract, a plant alkaloid, nitrosourea, a hormone, or a nucleoside or nucleotide analogue.

44. The use of claims 42 or 43, wherein the nucleic acid damaging agent or anti-proliferative agent comprises a drug.

45. The use of claims 42 or 43, wherein the nucleic acid damaging agent or anti-proliferative agent comprises a platinum containing drug.

46. The use of claims 42 or 43, wherein the nucleic acid damaging agent or anti-proliferative agent comprises cis-platin, carboplatin, nedaplatin, mitaplatin, satraplatin, picoplatin, triplatin, miriplatin, or oxaliplatin.

47. The use of any of claims 1 to 46, wherein the medicament further comprises a platinum containing drug, cis-platin, carboplatin, oxaliplatin, pemetrexed, gemcitabine, 5-fiuorouracil (5-FU), rebeccamycin, adriamycin (ADR), bleomycin (Bleo), pepleomycin, cisplatin, cisplatinum, or *cis*-diamminedichloroplatinum(II) (CDDP), oxaliplatin, or camptotecin (CPT), cyclophosphamide, azathioprine, cyclosporin A, prednisolone, melphalan, chlorambucil, mechlorethamine, busulphan, methotrexate, 6-mercaptopurine, thioguanine, 5-fluorouracil, cytosine arabinoside, AZT, 5-azacytidine (5-AZC) or a 5-azacytidine related compound, actinomycin D, mithramycin, mitomycin C, carmustine, lomustine, semustine, streptozotocin, hydroxyurea, cisplatin, mitotane, procarbazine, dacarbazine, a taxane, vinblastine, vincristine, doxorubicin, dibromomannitol, radiation or a radioisotope.

48. The use of claim 47, wherein the radiation comprises UVradiation, IR radiation, Xray, or alpha-, beta- or gamma-radiation.

49. The use of claim 46, wherein the radioisotope comprises I^{131}, I^{125}, Sr^{89}, Sm^{153}, Y^{90}, or Lu^{177}.

50. The use of any of claims 1-13, wherein the cell proliferative disorder comprises a tumor or cancer.

51. The use of claim 50, wherein the cell proliferative disorder comprises a metastatic tumor or cancer.

52. The use of claim 50 or 51, wherein the tumor or cancer comprises a lung tumor or cancer.

53. The use of claim 50 or 51, wherein the lung tumor or cancer comprises a small cell or non-small cell lung cancer.

54. The use of claim 50 or 51, wherein the lung tumor or cancer comprises an adenocarcinoma, squamous cell carcinoma or a large cell carcinoma.

55. The use of claim 50 or 51, wherein the tumor or cancer comprises a carcinoma, sarcoma, lymphoma, leukemia, adenoma, adenocarcinoma, melanoma, glioma, glioblastoma, meningioma, neuroblastoma, retinoblastoma, astrocytoma, oligodendrocytoma, mesothelioma, reticuloendothelial, lymphatic or haematopoietic neoplasia, tumor, cancer or malignancy.

56. The use of claim 50 or 51, wherein the sarcoma comprises a lymphosarcoma, liposarcoma, osteosarcoma, chondrosarcoma, leiomyosarcoma, rhabdomyosarcoma or fibrosarcoma.

57. The use of claim 55, wherein the haematopoietic neoplasia, tumor, cancer or malignancy comprises a myeloma, lymphoma or leukemia.

58. The use of claim 50 or 51, wherein the tumor or cancer comprises a lung, thyroid, head or neck, nasopharynx, throat, nose or sinuses, brain, spine, breast, adrenal gland, pituitary gland, thyroid, lymph, gastrointestinal (mouth, esophagus, stomach, duodenum, ileum, jejunum (small intestine), colon, rectum), genito-urinary tract (uterus, ovary, cervix, endometrial, bladder, testicle, penis, prostate), kidney, pancreas, liver, bone, bone marrow, lymph, blood, muscle, or skin neoplasia, tumor, or cancer.

59. The use of claim 50 or 51, wherein the tumor or cancer comprises a breast cancer, prostate cancer, pancreas cancer, gastric cancer, pleural mesothelioma, colon cancer, rectal cancer, large bowel cancer, small intestinal cancer, esophageal cancer, duodenal cancer, lingual cancer, pharyngeal cancer, salivary gland cancer, cerebral tumor, schwanoma, liver cancer, kidney cancer, bile duct cancer, endometrial cancer, cervical cancer, uterine body cancer, ovarian cancer, bladder cancer, urethral cancer, skin cancer, angioma, malignant lymphoma, malignant melanoma, thyroid cancer, parathyroid cancer, nasal cancer, paranasal cancer, auditory organ cancer, carcinoma of oral floor, laryngeal cancer, parotid cancer, submandibular cancer, bone tumor, angiofibroma, retinal sarcoma, penile cancer, testicular tumor, pediatric solid cancer, Kaposi's sarcoma, tumor of maxillary sinus, fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, lymphoma, multiple myeloma or leukemia.

60. The use of any of claims 1-59, wherein the mammal is a human.

61. The use of any of claims 2-59, wherein the peptide compound comprises: (d-Bpa)(d-Ser)(d-Trp)(d-Ser)(d-Phe-2,3,4,5,6-F)(d-Cha)(d-Arg)(d-Arg)(d-Arg)(d-Gln)(d-Arg)(d-Arg), or (d-Arg)(d-Arg)(d-Arg)(d-Gln)(d-Arg)(d-Arg)(d-Bpa)(d-Ser)(d-Trp)(d-Ser)(d-Phe-2,3,4,5,6-F)(d-Cha).

62. The use of any of claims 50-59, wherein the amount of the peptide compound to be administered is effective to treat the tumor or cancer.

63. The use of any of claims 50-59, wherein the medicament inhibits or reduces relapse, growth, progression, worsening or metastasis of the tumor or cancer.

64. The use of any of claims 1-59, wherein the medicament results in partial or complete destruction of neoplasia, tumor, cancer or malignant cell mass, volume, size or numbers of cells, stimulating, inducing or increasing neoplasia, tumor, cancer or malignant cell necrosis, lysis or apoptosis, reducing neoplasia, tumor, cancer or

malignancy volume size, cell mass, inhibiting or preventing progression or an increase in neoplasia, tumor, cancer or malignancy volume, mass, size or cell numbers, or prolonging lifespan.

65. The use of any of claims 1-59, wherein the medicament results in reducing or decreasing severity, duration or frequency of an adverse symptom or complication associated with or caused by neoplasia, tumor, cancer or malignancy.

66. The use of any of claims 1-59, wherein the medicament results in reducing or decreasing pain, discomfort, nausea, weakness or lethargy, or results in increased energy, appetite, improved mobility or psychological well being.

67. The use of any of claims 1-59, wherein the medicament results in stimulating, inducing or increasing CD8 (=CD45+CD8+) T cell population in neoplasia, tumor, cancer or malignancy.

68. The use of any of claims 1-59, wherein the medicament results in reducing or decreasing M2 macrophage (=F4/80+ CD206+) population in neoplasia, tumor, cancer or malignancy.