Claims:

1. A process for *in vitro* expansion of antigen specific T cells, such as autologous antigen specific T cells comprising the steps:

   a) culturing a population of autologous PBMC cells in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR a peptide/peptide mix relevant to a target antigen(s), and

      ii) at least one cytokine, and

   b) culturing a population of T cells from step a) in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR autologous antigen presenting T cells (T-APC's) cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) and an artificial co-stimulatory factor, and

      ii) optionally a cytokine, and

   characterized in that the process does not employ live virus and/or viral vectors or the use of DNA or RNA encoding antigens in the expansion of the relevant T cell population.

2. A process according to claim 1 wherein step b) is performed two or more times (such as 3, 4, 5 times or more) until sufficient quantities of the relevant T cell population are obtained.
3. A process according to claim 1 or 2 wherein the culturing of step a) is performed for 12 days or less.
4. A process according to any one of claims 1 to 3, wherein the culturing step of step b) is performed for 12 days or less.
5. A process according to any one of claims 1 to 4, wherein culturing is performed in a vessel comprising a gas permeable culture surface.
6. A process according to any one of claims 1 to 5, wherein the T cells expanded are specific to an Epstein-Barr Virus, Vaccinia Virus or Varicella Zoster Virus antigen or antigens, such as EBV.
7. A process according to any one of claims 1 to 6, wherein the peptides of step a) and/or b) comprise between 2 and 1000 peptides, for example 2 to 500 peptides, 2 to 300 peptides or 2 to 100 peptides.
8. A process according to any one of claims 1 to 7, wherein the peptides of step a) and/or b) overlap, for example by 2, 3, 4, ,5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more amino acids.
9. A process according to any one of claims 1 to 8, wherein the peptides of step a) and/or b) are about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids in length, such as 15 amino acids in length.
10. A process according to any one of claims 1 to 9, wherein the peptides of part a) and/or b) cover part or the full length of the antigen LMP1.
11. A process according to any one of claims 1 to 10, wherein the peptides of part a) and/or b) cover part or the full length of the antigen LMP2.
12. A process according to any one of claims 1 to 11, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen EBNA1.
13. A process according to any one of claims 1 to 12, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen BARF1.

14. A process according to any one of claims 1 to 13, wherein the cytokine present in step a) is IL-4.
15. A process according to any one of claims 1 to 14, wherein the cytokine present in step a) is IL-7.
16 A process according to any one of claims 1 to 15, wherein the cytokine present in step b) is IL-15.
17. A process according to any one of claims 1 to 15, wherein the artificial co-stimulatory is an engineered cell line, such as an aK562 cell, with one or more relevant protein or protein fragments present on the cell surface.
18. A process according to claim 17, wherein the protein or protein fragments are independently selected from CD80, CD86, CD83, OX-40 ligand and 41BB-ligand.
19. A process according to claim 18, wherein all of the said protein or protein fragments are present on the surface of the co-stimulatory cell.
20. A process according to any one of claims 1 to 19, wherein the process is performed in a GRex™ system.
21. An expanded autologous or allogenic T cell product obtainable or obtained from a process as defined in any one of claims 1 to 20.
22. An expanded autologous or allogenic T cell product according to claim 21, wherein one or more target cell populations has comparable target antigen specificity compared to cells expanded employing viral vectors and re-stimulated with EBV-LCLs that over-express certain target antigens.
23. An expanded autologous or allogenic T cell product according to claim 21 or 22, wherein one or more of target cell populations has higher target-antigen-specificity at a given timepoint than cells expanded employing viral vectors and re-stimulated with EBV-LCLs that over-express certain target antigens.
24. A pharmaceutical composition comprising an expanded T cell product as defined in any one of claims 21 to 23, and an excipient, carrier, stabiliser, surfactant or other non-therapeutically active component.
25. A method of treating a patient, such as an immunosuppressed patient, for viral infection or cancer induced by a virus by administration of an appropriate dose of an expanded T cell product as defined in any one of claims 21 to 23 or pharmaceutical composition as defined in claim 24.
26. Use of an engineered cell line such as an aK562 cell as an artificial co-stimulatory factor without concomitant presentation of antigen thereon, in the antigen specific expansion of T cells, such as autologous T cells.
27. Use of dendritic cells pulsed with antigen-peptide/peptide mixes for the expansion of antigen specific T cells.
28. Use of T-APCs pulsed with antigen-peptide/peptide mixes for the expansion of antigen specific T cells.
29. Use of antigen-peptide mixes with PBMCs for the expansion of antigen specific T cells.

AMENDED CLAIMS
received by the International Bureau on 05 November 2012 (05.11.2012)

Claims:

1. A process for *in vitro* expansion of antigen specific T cells, such as autologous antigen specific T cells comprising the steps:

   a) culturing a population of autologous PBMC cells in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR a peptide/peptide mix relevant to a target antigen(s), and

      ii) at least one cytokine, and

   b) culturing a population of T cells from step a) in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR autologous antigen presenting T cells (T-APC's) cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) and an artificial co-stimulatory factor, and

      ii) optionally a cytokine, and

   characterized in that the process does not employ live virus and/or viral vectors or the use of DNA or RNA encoding antigens in the expansion of the relevant T cell population.

2. A process according to claim 1 wherein step b) is performed two or more times (such as 3, 4, 5 times or more) until sufficient quantities of the relevant T cell population are obtained.
3. A process according to claim 1 or 2 wherein the culturing of step a) is performed for 12 days or less.
4. A process according to any one of claims 1 to 3, wherein the culturing step of step b) is performed for 12 days or less.
5. A process according to any one of claims 1 to 4, wherein culturing is performed in a vessel comprising a gas permeable culture surface.
6. A process according to any one of claims 1 to 5, wherein the T cells expanded are specific to a viral antigen or antigens of Epstein-Barr Virus, Vaccinia Virus or Varicella Zoster Virus, such as EBV.
7. A process according to any one of claims 1 to 6, wherein the peptides of step a) and/or b) comprise between 2 and 1000 peptides, for example 2 to 500 peptides, 2 to 300 peptides or 2 to 100 peptides.
8. A process according to any one of claims 1 to 7, wherein the peptides of step a) and/or b) overlap, for example by 2, 3, 4, ,5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more amino acids.
9. A process according to any one of claims 1 to 8, wherein the peptides of step a) and/or b) are about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids in length, such as 15 amino acids in length.
10. A process according to any one of claims 1 to 9, wherein the peptides of part a) and/or b) cover part or the full length of the antigen LMP1.
11. A process according to any one of claims 1 to 10, wherein the peptides of part a) and/or b) cover part or the full length of the antigen LMP2.
12. A process according to any one of claims 1 to 11, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen EBNA1.
13. A process according to any one of claims 1 to 12, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen BARF1.

Claims:

1. A process for *in vitro* expansion of antigen specific T cells, such as autologous antigen specific T cells comprising the steps:

   a) culturing a population of autologous PBMC cells in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR a peptide/peptide mix relevant to a target antigen(s), and

      ii) at least one cytokine, and

   b) culturing a population of T cells from step a) in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR autologous antigen presenting T cells (T-APC's) cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) and an artificial co-stimulatory factor, and

      ii) optionally a cytokine, and

   characterized in that the process does not employ live virus and/or viral vectors or the use of DNA or RNA encoding antigens in the expansion of the relevant T cell population.

2. A process according to claim 1 wherein step b) is performed two or more times (such as 3, 4, 5 times or more) until sufficient quantities of the relevant T cell population are obtained.
3. A process according to claim 1 or 2 wherein the culturing of step a) is performed for 12 days or less.
4. A process according to any one of claims 1 to 3, wherein the culturing step of step b) is performed for 12 days or less.
5. A process according to any one of claims 1 to 4, wherein culturing is performed in a vessel comprising a gas permeable culture surface.
6. A process according to any one of claims 1 to 5, wherein the T cells expanded are specific to ~~an~~ viral antigen or antigens of Epstein-Barr Virus, Vaccinia Virus or Varicella Zoster Virus ~~antigen or antigens~~, such as EBV.
7. A process according to any one of claims 1 to 6, wherein the peptides of step a) and/or b) comprise between 2 and 1000 peptides, for example 2 to 500 peptides, 2 to 300 peptides or 2 to 100 peptides.
8. A process according to any one of claims 1 to 7, wherein the peptides of step a) and/or b) overlap, for example by 2, 3, 4, ,5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more amino acids.
9. A process according to any one of claims 1 to 8, wherein the peptides of step a) and/or b) are about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids in length, such as 15 amino acids in length.
10. A process according to any one of claims 1 to 9, wherein the peptides of part a) and/or b) cover part or the full length of the antigen LMP1.
11. A process according to any one of claims 1 to 10, wherein the peptides of part a) and/or b) cover part or the full length of the antigen LMP2.
12. A process according to any one of claims 1 to 11, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen EBNA1.

13. A process according to any one of claims 1 to 12, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen BARF1.

Claims:

1. A process for *in vitro* expansion of antigen specific T cells, such as autologous antigen specific T cells comprising the steps:

   a) culturing a population of autologous PBMC cells in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR a peptide/peptide mix relevant to a target antigen(s), and

      ii) at least one cytokine, and

   b) culturing a population of T cells from step a) in the presence of:

      i) dendritic cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) OR autologous PBMC cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) and an artificial co-stimulatory factor, and

      ii) optionally a cytokine(s), and

   wherein the process does not employ live virus and/or viral vectors or the use of DNA or RNA encoding antigens in the expansion of the relevant T cell population.

2. A process according to claim 1 wherein step b) is performed two or more times, such as 3, 4, 5 times or more, until sufficient quantities of the relevant T cell population are obtained.
3. A process according to claim 1 or 2 wherein the culturing of step a) and/or step b) is performed for 12 days or less.
4. A process according to any one of claims 1 to 3, wherein culturing is performed in a vessel comprising a gas permeable culture surface.
5. A process according to any one of claims 1 to 4, wherein the T cells expanded are specific to a viral antigen or antigens of Epstein-Barr Virus, Vaccinia Virus or Varicella Zoster Virus antigen, such as EBV.
6. A process according to any one of claims 1 to 5, wherein the peptides of step a) and/or b) comprise between 2 and 1000 peptides, 2 to 500 peptides, 2 to 300 peptides or 2 to 100 peptides.
7. A process according to any one of claims 1 to 6, wherein the peptides of step a) and/or b) overlap, by 2, 3, 4, ,5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more amino acids.
8. A process according to any one of claims 1 to 7, wherein the peptides of step a) and/or b) are 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids in length.
9. A process according to any one of claims 1 to 8, wherein the peptides of part a) and/or b) independently cover part or the full length of the antigen LMP1 and/or cover part or the full length of the antigen LMP2.
10. A process according to any one of claims 1 to 9, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen EBNA1.
11. A process according to any one of claims 1 to 10, wherein the peptides of part a) and/or b) cover part of or the full length of the antigen BARF1.
12. A process according to any one of claims 1 to 11, wherein the cytokine present in step a) is IL-4 and/or IL-7.

13. A process according to any one of claims 1 to 12, wherein the cytokine present in step b) is IL-15.
14. A process according to any one of claims 1 to 13, wherein the artificial co-stimulatory is an engineered cell line, such as an aK562 cell, with one or more relevant protein or protein fragments present on the cell surface.
15. A process according to claim 14, wherein the protein or protein fragments are independently selected from CD80, CD86, CD83, OX-40 ligand and 41BB-ligand.
16. A process according to claim 15, wherein all of the said protein or protein fragments are present on the surface of the co-stimulatory cell.
17. A process according to any one of claims 1 to 16, wherein the process is performed in a GRex™ system.
18. A process according to any one of claims 1 to 17, wherein autologous antigen presenting T cells which have been pulsed with a peptide/peptide mix relevant to a target antigen(s) and an artificial co-stimulatory factor are used in step b).