disease), chronic inflammatory diseases, autoimmune diseases, unwanted immune response against therapeutic proteins or allergies in a patient in need thereof.

In one aspect of the present disclosure, there is provided an isolated population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ T regulatory (Treg) cells, wherein said Treg cells are preferably $GITR^+$ and/or $Foxp3^+$.

In another aspect of the present disclosure, there is provided a method for detecting and/or isolating $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells from a biological sample containing human peripheral blood mononuclear cells (PBMCs) or lymphocytes, wherein said Treg cells optionally are $GITR^+$ and/or $Foxp3^+$, comprising the following steps of: (a) contacting said population of human PBMCs or lymphocytes with means useful for isolating a population of human $CD8^+CD45RC^{low}$ Treg cells, optionally with means useful for isolating a population of $GITR^+$ and/or $Foxp3^+$ $CD8^+CD45RC^{low}$ Treg cells, wherein the means useful for isolating the population of human $CD8^+CD45RC^{low}$ Treg cells are binding partners, preferably antibodies, to suitable cell surfaces molecules or markers selected from the group comprising CD3, CD8 and CD45RC; (b) contacting the isolated population of human $CD8^+CD45RC^{low}$ Treg cells obtained at step (a) with means useful for isolating $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells, and wherein the means useful for isolating $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells are bispecific antibodies which binds to one cytokine selected from the group comprising IFNγ, IL-10 and IL-34 and to a cell surface molecule selected from the group comprising CD3, CD8 and CD45RC.

In yet another aspect of the present disclosure, there is provided a method for expanding $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells, said Treg cells optionally being $GITR^+$ and/or $Foxp3^+$, comprising a step of contacting an isolated population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells with a culture medium suitable for expanding Treg cells.

In a further aspect of the present disclosure, there is provided a method for producing a population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells comprising:

- isolating $CD8^+GITR^+$ Treg cells from a biological sample containing human peripheral blood mononuclear cells (PBMCs) or lymphocytes, optionally isolating $CD8^+CD45RC^{low}GITR^+$ Treg cells from a biological sample containing human peripheral blood mononuclear cells (PBMCs) or lymphocytes,
- optionally freezing and subsequently thawing the isolated Treg cells, and
- expanding said cells in culture.

In another aspect of the present disclosure, there is provided an isolated population of expanded $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells, wherein preferably said Treg cells are $GITR^+$ and/or $Foxp3^+$.

In yet another aspect of the present disclosure, there is provided a pharmaceutical composition comprising an isolated population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells as defined herein or an isolated population of expanded $IFN\gamma^+IL$-

CLAIMS:

1. An isolated population of IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} T regulatory (Treg) cells, wherein said Treg cells are preferably GITR$^+$ and/or Foxp3$^+$.

2. The isolated population according to claim **1**, wherein said Treg cells are genetically modified Treg cells comprising a chimeric antigen receptor (CAR) or a chimeric autoantibody receptor (CAAR).

3. A method for detecting and/or isolating IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells from a biological sample containing human peripheral blood mononuclear cells (PBMCs) or lymphocytes, wherein said Treg cells optionally are GITR$^+$ and/or Foxp3$^+$, comprising the following steps of: (a) contacting said population of human PBMCs or lymphocytes with means useful for isolating a population of human CD8$^+$CD45RC^{low} Treg cells, optionally with means useful for isolating a population of GITR$^+$ and/or Foxp3$^+$ CD8$^+$CD45RC^{low} Treg cells, wherein the means useful for isolating the population of human CD8$^+$CD45RC^{low} Treg cells are binding partners, preferably antibodies, to suitable cell surfaces molecules or markers selected from the group comprising CD3, CD8 and CD45RC; (b) contacting the isolated population of human CD8$^+$CD45RC^{low} Treg cells obtained at step (a) with means useful for isolating IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells, and wherein the means useful for isolating IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells are bispecific antibodies which binds to one cytokine selected from the group comprising IFNγ, IL-10 and IL-34 and to a cell surface molecule selected from the group comprising CD3, CD8 and CD45RC.

4. The method according to claim **3**, wherein the means useful for isolating the population of human CD8$^+$CD45RC^{low} Treg cells are a combination of at least three antibodies consisting of a monoclonal anti-human CD3 antibody, a monoclonal anti-human CD8 antibody and a monoclonal anti-human CD45RC antibody, optionally further comprising an anti-human GITR antibody, and wherein the means useful for isolating IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells are a combination of at least two bispecific antibodies selected from the group consisting of a bispecific antibody which binds to IFNγ and to a cell surface molecule specific for T cells selected from the group comprising CD3, CD8, and CD45, a bispecific antibody which binds to IL-10 and to a cell surface molecule specific for T cells selected from the group comprising CD3, CD8 and CD45 and a bispecific antibody which binds to IL-34 and to a cell surface molecule specific for T cells selected from the group comprising CD3, CD8 and CD45.

5. A method for expanding IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells, said Treg cells optionally being GITR$^+$ and/or Foxp3$^+$, comprising a step of contacting an isolated population of IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells with a culture medium suitable for expanding Treg cells.

6. The method according to claim **5**, wherein the isolated population of IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells is frozen and subsequently thawed before being contacted with a culture medium suitable for expanding Treg cells.

7. The method according to claim **5** or **6**, wherein said culture medium suitable for expanding Treg cells comprises at least an antigen-specific stimulating agent selected from the group consisting of antigens, cells, MHC polymers and antibodies.

8. The method according to any one of claims **5** to **7**, wherein said culture medium comprises at least one cytokine, preferably wherein said culture medium comprises an amount of interleukin-2 (IL-2) and/or an amount of interleukin-15 (IL-15).

9. A method for producing a population of IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells comprising:

- isolating CD8$^+$GITR$^+$ Treg cells from a biological sample containing human peripheral blood mononuclear cells (PBMCs) or lymphocytes, optionally isolating CD8$^+$CD45RC^{low}GITR$^+$ Treg cells from a biological sample containing human peripheral blood mononuclear cells (PBMCs) or lymphocytes,
- optionally freezing and subsequently thawing the isolated Treg cells, and
- expanding said cells in culture.

10. An isolated population of expanded IFNγ$^+$IL-10$^+$IL-34$^+$ secreting human CD8$^+$CD45RC^{low} Treg cells, wherein preferably said Treg cells are GITR$^+$ and/or Foxp3$^+$.

11. The isolated population according to claim **10**, wherein said Treg cells are antigen-specific and/or are genetically modified Treg cells comprising a CAR or a CAAR.

12. A pharmaceutical composition comprising an isolated population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells according to claim **1** or claim **2** or an isolated population of expanded $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells according to claim **10** or claim **11** and at least one pharmaceutically acceptable carrier.

13. An isolated population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells according to claim **1** or claim **2** or an isolated population of expanded $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells according to claim **10** or claim **11** for use as a medicament.

14. Use of an isolated population of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells according to claim **1** or claim **2** or of an isolated population of expanded $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells according to claim **10** or claim **11** for the manufacture of a medicament for preventing or treating transplant rejection, GVHD, chronic inflammatory diseases, autoimmune diseases, unwanted immune response against therapeutic proteins or allergies in a patient in need thereof.

15. An *in vitro* method for determining whether a patient is at risk of transplant rejection, GVHD, chronic inflammatory diseases, autoimmune diseases, unwanted immune response against therapeutic proteins or allergies, comprising a step of determining the presence of $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells in a biological sample obtained from said patient by a method according to claim **3** or claim **4**, wherein the presence of a $IFN\gamma^+IL\text{-}10^+IL\text{-}34^+$ secreting human $CD8^+CD45RC^{low}$ Treg cells is indicative of a reduced risk of transplant rejection, GVHD, chronic inflammatory diseases, autoimmune diseases, unwanted immune response against therapeutic proteins or allergies.