Claims

1. Use of a composition in the manufacture of a medicament for treating a mammal suffering from or susceptible to an immune reaction to drug treatment, wherein the composition comprises antigen presenting cells obtained from the mammal and are treated ex-vivo with an IDO-inducing agent in the presence of said drug or an epitope containing fragment thereof.

2. The use according to claim 1 where the mammal is a human.

3. The use according to claim 1 or claim 2 wherein the drug is a biological drug.

4. The use according to claim 3 wherein the drug is FVIII.

5. The use according to claim 3 wherein the drug is Factor IX.

6. The use according to claim 3 wherein the drug is an antibody.

7. The use according to any one of claims 1 to 6 wherein the antigen presenting cells are dendritic cells.

8. The use according to claim 7 wherein the dendritic cells are bone marrow-derived dendritic cells, dendritic cells generated from CD34+ hematopoietic progenitor cells or dendritic cells generated from peripheral blood mononuclear cells.

9. The use according to any one of claims 1 to 8 wherein the IDO-inducing agent is zebularine or an analogue or salt thereof.

10. The use according to claim 9 wherein the agent is zebularine.

11. The use according to any one of claims 1 to 8 wherein the agent is selected from cytidine analogues (e.g. 5-methylcytidine, azacytidine or deoxyazacytidine), histone deacetylase inhibitors (e.g. valproic acid or salts thereof such as sodium valproate, trichostatin A or vorinostate (SAHA)), vitamin D3 analogues (e.g. calcitriol), interferon gamma analogues, other interferons (e.g. interferon alpha, interferon B1 or interferon-tau), toll like receptor ligands (e.g. CpG containing DNA oligonucleotides or lipopolysaccharides), gonadotropin receptor signalling hormones (e.g. recombinant human gonadotropin (rhCG) or prolactin), prostaglandin E2 analogues, IDO stabilizers (e.g. TGF-b or IL-10), soluble CTLA4 conjugates (e.g. CTLA4-Ig such as abatacept) and glycocorticoids (e.g. dexamethasone).

12. The use according to claim 11 wherein the IDO-inducing agent is selected from azacytidine and deoxyazacytidine.

13. The use according to claims 1 to 8 wherein the IDO–inducing agent comprises two or more agents selected from (i) zebularine and IFN-gamma, (ii) IFN-gamma and valproic acid, (iii) zebularine, IFN-gamma and valproic acid, (iv) human chorionic gonadotropin (hCG) and zebularine, (v) hCG and IFN-gamma, (vi) zebularine and IFN-A, (vii) zebularine, IFN-gamma and IFN-A, (viii) zebularine, IFN-gamma and TGF-beta, and (ix) zebularine, IFN-gamma, IFN-A, and TGF-beta.

14. A method of inducing IDO in a cell culture by a method comprising *ex-vivo* treating antigen presenting cells obtained from a mammal with an agent which induces IDO in said antigen presenting cells in the presence of a drug or an epitope containing fragment thereof.

15. A method according to claim 14 wherein the antigen presenting cells are dendritic cells.

16. A method according to claim 14 or claim 15 wherein the drug is a biological drug.

17. A method according to claim 16 wherein the drug is FVIII.

18. A method according to claim 16 wherein the drug is an antibody.

19. A method according to any one of claims 14 to 18 wherein the agent is zebularine or an analogue or salt thereof.

20. A method according to any one of claims 14 to 18 wherein the agent is selected from azacytidine and deoxyazacytidine.

21. Antigen presenting cells in which IDO has been induced obtained by the method of any one of claims 14 to 20.

22. Antigen presenting cells according to claim 21 for use in a method of treating a mammal suffering from or susceptible to an immune reaction to drug treatment comprising the raising of anti-drug antibodies whereby according to said method said cells are transferred back to said mammal thereby to establish immune tolerance to the drug.