CLAIMS

1. An immunodeficient mouse model of human humoral and cellular immunity, comprising a transgene encoding human interleukin-3 (IL-3), a transgene encoding human granulocyte/macrophage-colony stimulating factor 2 (GM-CSF), a transgene encoding human stem cell factor (SCF), and a transgene encoding human IL-15; and obtained by myeloablative treatment and engraftment of peripheral blood mononuclear cells (hPBMCs).
2. The mouse model of claim 1, obtained by myeloablative treatment comprising irradiation.
3. The mouse model of claim 2, obtained by irradiation comprising gamma irradiation (cGy).
4. The mouse model of claim 3, obtained by irradiation comprising is ≤ 150 cGy.
5. The mouse model of claim 4, obtained by irradiation comprising is ≤ 100 cGy.
6. The mouse model of claim 5, obtained by irradiation comprising is about 50 to about 100 cGy.
7. The mouse model of claim 6, obtained by irradiation comprising is 40-60 cGy.
8. The mouse model of claim 7, obtained by irradiation comprising 50 cGy.
9. The mouse model of any one of the preceding claims, obtained by engraftment of fewer than $1x10^7$ of hPBMCs.
10. The mouse model of claim 9, wherein $0.5x10^6$ – $5x10^6$ of hPBMCs was administered to the immunodeficient mouse.
11. The mouse model of claim 10, obtained by engraftment of $4x10^6$ of hPBMCs.
12. The mouse model of any one of the preceding claims, obtained by engraftment of hPBMCs within 3 days of the myeloablative treatment.
13. The mouse model of claim 12, obtained by engraftment of hPBMCs on the same day the myeloablative treatment.
14. The mouse model of claim 13, obtained by engraftment of hPBMCs within 6 hours of the myeloablative treatment.
15. The mouse model of claim 14, obtained by engraftment of hPBMCs at the same time as the myeloablative treatment.
16. The mouse model of any one of the preceding claims, obtained by further engraftment of human diseased cells.

17. The mouse model of any one of the preceding claims, wherein the mouse is to be administered a human therapeutic or prophylactic agent.

18. The mouse model of claim 17, wherein the mouse is to be administered a human immunomodulatory agent.

19. The mouse model of claim 18, wherein the mouse is to be administered a monoclonal antibody.

20. The mouse model of claim 18, wherein the mouse is to be administered a cellular therapy, optionally a T cell therapy.

21. The mouse model of claim 17, wherein the mouse is to be administered a vaccine.

22. The mouse model of claim 21, wherein the mouse is to be administered a protein antigen or a nucleic acid encoding a protein antigen, optionally a cancer antigen or a pathogenic antigen.

23. The mouse model of any one of claims 17-22, wherein the mouse is to be administered a human therapeutic agent within 30 days of the myeloablative treatment.

24. The mouse model of claim 23, wherein the mouse is to be administered a human therapeutic agent within 28 days of the myeloablative treatment.

25. The mouse model of claim 23, wherein the mouse is to be administered a human therapeutic agent within 21 days of the myeloablative treatment.

26. The mouse model of claim 25, wherein the mouse is to be administered a human therapeutic agent within 14 days of the myeloablative treatment.

27. A method comprising assaying an isolated sample, optionally a blood sample, from the mouse model of any one of the preceding claims for one or more human cytokines.

28. The method of claim 27, wherein the one or more human cytokines are selected from interferon gamma (IFN-γ), interleukin (IL)-2, IL-4, IL-6, IL-10, and tumor necrosis factor alpha (TNFα).

29. A method comprising assaying an isolated sample, optionally an isolated blood sample, from the mouse model of any one of the preceding claims for one or more human immunoglobulins.

30. The method of claim 29, wherein the one or more human immunoglobulins are selected from IgM, IgA, IgG, optionally IgG1, IgG2, IgG3, and IgG4.

31. A method comprising assaying an isolated sample, optionally an isolated blood sample, from the mouse model of any one of the preceding claims for one or more

anti-drug antibodies.

32. A mouse model of human humoral and cellular immunity of any one of claims 1-26, wherein the mouse model further comprises (a) human cytokines selected from interferon gamma (IFN-γ), interleukin (IL)-2, IL-4, IL-6, IL-10, and tumor necrosis factor alpha (TNFα) and/or (b) one or more human immunoglobulins.

33. An immunodeficient mouse comprising a transgene encoding human interleukin-3 (IL-3), a transgene encoding human granulocyte/macrophage-colony stimulating factor 2 (GM-CSF), a transgene encoding human stem cell factor (SCF), and a transgene encoding human IL-15.

34. The immunodeficient mouse of claim 33, wherein the immunodeficient mouse has a non-obese diabetic genetic background.

35. The immunodeficient mouse of claim 33 or 34, wherein the immunodeficient mouse has a severe combined immune deficiency mutation (*Prkdc*^{scid}).

36. The immunodeficient mouse of any one of claims 33-35, wherein the immunodeficient mouse has a null allele of the IL2 receptor common gamma chain (*IL2rg*^{null}).

37. The immunodeficient mouse of any one of claims 33-36, wherein the immunodeficient mouse has a NOD-*scid* IL2Rgamma^{null} genetic background.

38. The immunodeficient mouse of any one of claims 33-37, wherein the immunodeficient mouse is to be exposed to myeloablative treatment.

39. The immunodeficient mouse of claim 38, wherein the immunodeficient mouse is to be exposed to myeloablative treatment comprising irradiation.

40. The immunodeficient mouse of any one of claims 33-39, wherein cells of the immunodeficient mouse produce human IgM, IgG1, IgG2, IgG3, and IgG4.

41. The immunodeficient mouse of claim 40, wherein the cells of the immunodeficient mouse produce 6000-16000 μg/mL of human IgG.

42. The immunodeficient mouse of claim 40 or 41, wherein cells of the immunodeficient mouse produce 1000-2000 μl/mL of human IgM.

43. The immunodeficient mouse of any one of claims 39-42, wherein cells of the immunodeficient mouse produce 1500-2500 μl/mL of human IgG1.

44. The immunodeficient mouse of any one of claims 39-43, wherein cells of the immunodeficient mouse produce 500-1500 μl/mL of human IgG2.

45. The immunodeficient mouse of any one of claims 39-44, wherein cells of the

immunodeficient mouse produce 150-205 µl/mL of human IgG3.

46. The immunodeficient mouse of any one of claims 39-45, wherein cells of the immunodeficient mouse produce 50-1000 µl/mL of human IgG4.

47. The immunodeficient mouse of any one of claims 32-46, wherein the immunodeficient mouse produces human $CD3^+$, $CD4^+$, $CD8^+$ and $CD19^+$ cells.