

CLAIMS

1. A NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Wjl}/SzJ (NOD-*scid*-IL2 γ ^{null}, NSG) mouse genetically modified such that the NSG mouse lacks functional major histocompatibility complex I (MHC I) and lacks functional major histocompatibility complex II (MHC II).

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2. The genetically modified NSG mouse of claim 1, wherein the mouse is a NOD.Cg-*Prkdc*^{scid} *H2-K1*^{tm1Bpe} *H2-Ab1*^{em1Mvw} *H2-D1*^{tm1Bpe} *Il2rg*^{tm1Wjl}/SzJ (NSG-(*K*^b *D*^b)^{null} (*I*A^{null})) mouse.

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3. The genetically modified NSG mouse of claim 1, wherein the mouse is a NSG-RIP-DTR (*K*^b *D*^b)^{null} (*I*A^{null}) mouse.

4. The genetically modified NSG mouse of claim 1, wherein the mouse is a NOD.Cg-*B2m*^{tm1Unc} *Prkdc*^{scid} *H2*^{dlAb1-Ea} *Il2rg*^{tm1Wjl}/SzJ (NSG-*B2M*^{null} (*I*A *I*E^{null})) mouse.

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5. The genetically modified NSG mouse of any of claims 1, 2, 3 or 4, further comprising human immune cells.

6. The genetically modified NSG mouse of claim 5, wherein the human
20 immune cells are human peripheral blood mononuclear cells.

7. The genetically modified NSG mouse of claim 5, wherein the human immune cells are human T cells.

8. The genetically modified NSG mouse of any of claims 1 to 7, further
25 comprising human tumor cells.

9. An immunodeficient mouse genetically modified such that the mouse lacks functional major histocompatibility complex I (MHC I) and lacks functional major
30 histocompatibility complex II (MHC II), with the proviso that the immunodeficient mouse is not a NOD/Shi-*scid*-IL2 γ ^{null} mouse characterized by β 2m (component of MHC I) knockout and *I*A β (light chain of MHC II) knockout.

10. The genetically modified immunodeficient mouse of claim 9, further comprising human immune cells.

11. The genetically modified immunodeficient mouse of claim 10, wherein
5 the human immune cells are human peripheral blood mononuclear cells.

12. The genetically modified immunodeficient mouse of claim 10, wherein the human immune cells are human T cells.

10 13. The genetically modified NSG mouse of any of claims 9 to 12, further comprising human tumor cells.

14. A method for modeling an effect of a human immune system in a genetically modified immunodeficient mouse, comprising:

15 administering a test substance to the genetically modified immunodeficient mouse according to any of claims 5 to 8 or 10 to 13; and

assaying the effect of the human immune system in the genetically modified immunodeficient mouse.

20 15. The method of claim 14 wherein the test substance is an anti-cancer agent.

16. The method of claim 14 or 15, wherein the test substance is an immunotherapeutic agent.

25 17. The method of claim 14, 15, or 16 wherein the test substance is an anti-cancer immunotherapeutic agent.

18. The method of any one of claims 14 to 17, wherein the test substance is an immune checkpoint inhibitor.

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19. The method of claim 18, wherein the immune checkpoint inhibitor is a PD-1 inhibitor, PD-L1 inhibitor, or CTLA-4 inhibitor.

20. The method of claim 18 or 19, wherein the immune checkpoint inhibitor is atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab, or pembrolizumab, or the immune checkpoint inhibitor comprises an antigen-binding fragment of any one of the foregoing.