WHAT IS CLAIMED IS:

1. An immunoresponsive cell comprising:
   (a) an NKG2D polypeptide;
   (b) a fusion polypeptide comprising (i) a DNAX-activating 10 (DAP10) polypeptide, or a functional variant thereof and (ii) a DNAX-activating protein 12 (DAP12) polypeptide, or a functional variant thereof; and
   (c) a CXCR2 polypeptide.

2. The immunoresponsive cell of claim 1, wherein each of the NKG2D polypeptide, the DAP10 polypeptide, the DAP12 polypeptide, and the CXCR2 polypeptide is a mammalian polypeptide.

3. The immunoresponsive cell of claim 2, wherein each of the NKG2D polypeptide, the DAP10 polypeptide, the DAP12 polypeptide, and the CXCR2 polypeptide is a human polypeptide.

4. The immunoresponsive cell of any one of the preceding claims, wherein the amino acid sequence of the NKG2D polypeptide has at least about 85% sequence identity to the sequence of SEQ ID NO: 14.

5. The immunoresponsive cell of any one of the preceding claims, wherein the NKG2D polypeptide is a functional variant of the polypeptide having the amino acid sequence of SEQ ID NO: 14.

6. The immunoresponsive cell of claim 5, wherein the functional variant has one or more point mutations that add, delete, or substitute at least one of the amino acids of SEQ ID NO: 14.

7. The immunoresponsive cell of claim 5, wherein the functional variant is a truncated version of the polypeptide having the amino acid sequence of SEQ ID NO: 14.

8. The immunoresponsive cell of claim 5, wherein the functional variant is a chimeric NKG2D polypeptide.

9. The immunoresponsive cell of any one of the preceding claims, wherein the fusion polypeptide has the formula, from N-terminus to C-terminus:

A-B-C-D-E,

wherein

A is an optional N-terminal sequence;

B is a DAP10 polypeptide or functional variant thereof;

C is an optional linker sequence;

D is a DAP12 polypeptide or functional variant thereof; and

E is an optional C-terminal sequence.

10. The immunoresponsive cell of any one of the preceding claims, comprising the functional variant of DAP10 polypeptide, wherein the functional variant of DAP10 polypeptide comprises an amino acid sequence having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the DAP10 polypeptide of SEQ ID NO: 1.

11. The immunoresponsive cell of any one of the preceding claims, wherein the functional variant of DAP10 polypeptide is a functional variant of SEQ ID NO: 1 having one or more (i.e. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more) point mutations that add, delete, or substitute any of the amino acids of the DAP10 polypeptide of SEQ ID NO: 1.

12. The immunoresponsive cell of any one of the preceding claims, wherein the functional variant of DAP10 polypeptide is a truncated version of the polypeptide having the amino acid sequence of SEQ ID NO: 1.

13. The immunoresponsive cell of claim 12, wherein the truncated version of DAP10 comprises or consists of amino acids 19-93, 19-69, 1-71, 19-71, 19-48, 49-69, 49-93, or 70-93 of SEQ ID NO: 1.

14. The immunoresponsive cell of any one of claims 1-8, wherein the DAP10 polypeptide or the functional variant thereof comprises or consists of any one of SEQ ID NOs: 1-8.

15. The immunoresponsive cell of any one of the preceding claims, comprising the functional variant of DAP12 polypeptide, wherein the functional variant of DAP12

polypeptide comprises an amino acid sequence having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the DAP12 polypeptide of SEQ ID NO: 9.

16. The immunoresponsive cell of any of the preceding claims, wherein the functional variant of DAP12 polypeptide is a functional variant of SEQ ID NO: 9 having one or more (i.e. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more) point mutations that add, delete, or substitute any of the amino acids of the DAP12 polypeptide of SEQ ID NO: 9.

17. The immunoresponsive cell of any one of the preceding claims, wherein the functional variant of DAP12 polypeptide is a truncated version of the polypeptide having the amino acid sequence of SEQ ID NO: 9.

18. The immunoresponsive cell of claim 17, wherein the truncated version of DAP12 comprises or consists of amino acids 22-113, 62-113, 22-61, or 41-61 of SEQ ID NO: 9.

19. The immunoresponsive cell of any one of claims 1-14, wherein the DAP12 polypeptide or the functional variant thereof comprises or consists of any one of SEQ ID NOs: 9-13.

20. The immunoresponsive cell of any one of the preceding claims, wherein the DAP10 polypeptide or the functional variant thereof and the DAP12 polypeptide or the functional variant thereof are joined by a linker.

21. The immunoresponsive cell of claim 20, wherein the linker comprises or consists of the amino acid sequence recited in any of SEQ ID NOs: 18-46.

22. The immunoresponsive cell of claim 20 or claim 21, wherein the linker comprises or consists of the amino acid sequence recited in any of SEQ ID NOs: 33 or 38-44.

23. The immunoresponsive cell of any one of the preceding claims, wherein the fusion polypeptide comprises an N-terminal sequence.

24. The immunoresponsive cell of any one of the preceding claims, wherein the fusion polypeptide comprises a C-terminal sequence.

25. The immunoresponsive cell of claim 23 or claim 24, wherein the N-terminal or C-terminal sequence comprises one or more of a His-tag, FLAG-tag, Arg-tag, T7-tag, Strep-tag, S-tag, an AviTag^{TM}, an aptamer-tag, a myc tag, CD8α leader sequence, a 4-1BB endodomain, a V5 tag, or a CD27 endodomain.

26. The immunoresponsive cell of claim 25, wherein the N-terminal or C-terminal sequence comprises one or more of a CD8α leader sequence, a 4-1BB endodomain, or a CD27 endodomain.

27. The immunoresponsive cell of any one of the preceding claims, wherein the fusion polypeptide comprises or consists of the sequence of any one of SEQ ID NOs: 60 to 63.

28. The immunoresponsive cell of any one of claims 1-8, wherein the fusion polypeptide:

(a) does not comprise SEQ ID NO: 84; and/or

(b) does not comprise an anti-EpCAM peptide; and/or

(c) does not comprise SEQ ID NO: 85; and/or

(d) does not comprise SEQ ID NO: 86; and/or

(e) does not comprise both SEQ ID NO: 85 and SEQ ID NO: 86.

29. The immunoresponsive cell of any one of the preceding claims, wherein the fusion polypeptide comprises or consists of full length human DAP10 fused at its C-terminus to the endodomain of human DAP12 polypeptide, wherein the endodomain is encoded by amino acids 62-113 of human DAP12.

30. The immunoresponsive cell of any one of the preceding claims, wherein the fusion polypeptide has the sequence of SEQ ID NO: 60.

31. The immunoresponsive cell of any one of the preceding claims, wherein the amino acid sequence of the CXCR2 polypeptide has at least about 85% sequence identity to the sequence of SEQ ID NO: 87.

32. The immunoresponsive cell of claim 31, wherein the CXCR2 polypeptide has the amino acid sequence of SEQ ID NO: 87.

33. The immunoresponsive cell of any one of the preceding claims, wherein the immunoresponsive cell is a T-cell or a Natural Killer (NK) cell.

34. The immunoresponsive cell of claim 33, wherein the immunoresponsive cell is an αβ T-cell, a γδ T-cell, a $CD4^+$ T-cell, a $CD8^+$ T-cell, a Natural Killer T (NKT) cell, or any combination thereof.

35. A nucleic acid molecule encoding:

(a) an NKG2D polypeptide;

(b) a fusion polypeptide comprising (i) a DNAX-activating 10 (DAP10) polypeptide, or a functional variant thereof and (ii) a DNAX-activating protein 12 (DAP12) polypeptide, or a functional variant thereof; and

(c) a CXCR2 polypeptide.

36. The nucleic acid molecule of claim 35, wherein the nucleic acid molecule is a chimeric polynucleotide.

37. The nucleic acid molecule of claim 36, wherein the nucleic acid molecule encodes, from 5' to 3', (i) human DAP10 in frame with the endodomain of human DAP12; (ii) a first protease cleavage site; (iii) a first linker; (iv) a first ribosomal skip peptide; (v) human NKG2D; (vi) a second protease cleavage site; (viii) a second linker; (viii) a second ribosomal skip peptide; and (ix) human CXCR2.

38. The nucleic acid molecule of any one of claims 35-37, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 88.

39. The nucleic acid molecule of any one of claims 35-38, wherein the nucleic acid has the nucleotide sequence of SEQ ID NO: 91.

40. A vector comprising the nucleic acid sequence of any one of claims 35-39.

41. The vector of claim 40, wherein the vector is a lentiviral vector or a retroviral vector.

42. The vector of claim 41, wherein the vector is a SFG retroviral vector.

43. A method of making the immunoresponsive cell of any one of claims 1-34, comprising the steps of:

(a) transducing a T-cell or a natural killer cell with the nucleic acid molecule of any one of claims 35-39 or a vector of any one of claims 40-42; and

(b) culturing the T-cell or natural killer cell such that the transduced cell expresses a NKG2D polypeptide, a DAP10/DAP12 fusion polypeptide, and a CXCR2 polypeptide, wherein the NKG2D polypeptide and the DAP10/DAP12 fusion polypeptide associate in the cell membrane.

44. The immunoresponsive cell of any one of claims 1-34 for use in the treatment or prophylaxis of cancer.

45. The immunoresponsive cell for use of claim 44, wherein the immunoresponsive cells are manufactured from T or NK cells autologous to the subject to be treated.

46. The immunoresponsive cell for use of claim 44 or claim 45, wherein the cancer is a solid tumor cancer.

47. The immunoresponsive cell for use of claim 46, wherein the solid tumor cancer is selected from liver cancer, lung cancer, breast cancer, prostate cancer, lymphoid cancer, colon cancer, renal cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head and neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, thyroid cancer, cancer of the esophagus, cancer of the small intestine, or any combination thereof.

48. The immunoresponsive cell for use of claim 47, wherein the solid tumor cancer is ovarian cancer.

49. An immunoresponsive cell comprising:

(a) a chimeric NKG2D polypeptide comprising a human NKG2D extracellular domain or a variant thereof and a murine NKG2D transmembrane domain or a variant thereof;

(b) a CXCR2 polypeptide; and

(c) at least one DNAX-activating protein 12 (DAP12) polypeptide or a variant thereof and at least one DNAX-activating protein 10 (DAP10) polypeptide or variant thereof.

50. The immunoresponsive cell of claim 49, wherein the human NKG2D extracellular domain has the sequence set forth in SEQ ID NO: 95, SEQ ID NO: 96, or SEQ ID NO: 97.

51. The immunoresponsive cell of claim 49 or claim 50, wherein the murine NKG2D transmembrane domain has the sequence set forth in SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, or SEQ ID NO: 101.

52. The immunoresponsive cell of claim 49, wherein the chimeric NKG2D polypeptide comprises a variant of the human NKG2D extracellular domain, wherein the variant has at least 80% sequence identity to any of SEQ ID Nos: 95, 96, or 97.

53. The immunoresponsive cell of any one of claims 49-50 or claim 52, wherein the chimeric NKG2D polypeptide comprises a variant of the murine NKG2D transmembrane domain, wherein the variant has at least 80% sequence identity to any of SEQ ID NOs: 98, 99, 100, or 101.

54. The immunoresponsive cell of any one of claims 49-53, wherein the cell comprises a polypeptide that has at least 90% sequence identity to the sequence set forth in SEQ ID NO: 102.