

WHAT IS CLAIMED IS:

1. A method of promoting the activation and proliferation of a natural killer cell, the method comprising:

(a) contacting a natural killer cell in a liquid culture medium comprising an effective amount of a first multi-chain chimeric polypeptide for a first period of time under conditions that allow for the differentiation of the natural killer cell; and

(b) contacting the natural killer cell in a liquid culture medium comprising an effective amount of (i) a second multi-chain chimeric polypeptide, and (ii) an IgG1 antibody construct, for a second period of time under conditions that allow for the activation and proliferation of the natural killer cell,

wherein the first multi-chain chimeric polypeptide comprises:

a first chimeric polypeptide comprising a first target-binding domain, a soluble tissue factor domain, and a first domain of a pair of affinity domains, and

a second chimeric polypeptide comprising a second domain of a pair of affinity domains and a second target-binding domain,

wherein the first chimeric polypeptide and the second chimeric polypeptide in the first multi-chain chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains in the first multi-chain chimeric polypeptide, and the first target-binding domain and the second target-binding domain in the first multi-chain chimeric polypeptide each independently bind specifically to a receptor of IL-18 or a receptor of IL-12; and

wherein the second multi-chain chimeric polypeptide comprises:

a first chimeric polypeptide comprising a first target-binding domain, a linker domain, a first domain of a pair of affinity domains, and

a second chimeric polypeptide comprising a second domain of a pair of affinity domains, and a second target-binding domain,

wherein the first chimeric polypeptide and the second chimeric polypeptide in the second multi-chain chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains in the second multi-chain chimeric polypeptide; the first target-

binding domain and the second target-binding domain in the second multi-chain chimeric polypeptide each independently bind specifically to a receptor for IL-7 or a receptor for IL-21, and the IgG1 antibody construct comprises at least one antigen-binding domain that binds specifically to the linker domain.

2. The method of claim 1, wherein the first target-binding domain and the soluble tissue factor domain directly abut each other in the first chimeric polypeptide in the first multi-chain chimeric polypeptide.

3. The method of claim 1, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a linker sequence between the first target-binding domain and the soluble tissue factor domain in the first chimeric polypeptide.

4. The method of any one of claims 1-3, wherein the soluble tissue factor domain and the first domain of the pair of affinity domains in the first chimeric polypeptide in the first multi-chain chimeric polypeptide directly abut each other in the first chimeric polypeptide.

5. The method of any one of claims 1-3, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the first domain of the pair of affinity domains in the first chimeric polypeptide.

6. The method of any one of claims 1-5, wherein the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide in the first multi-chain chimeric polypeptide directly abut each other in the second chimeric polypeptide.

7. The method of any one of claims 1-5, wherein the second chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a linker sequence between the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide.

8. The method of any one of claims 1-7, wherein the soluble tissue factor domain is a soluble human tissue factor domain.

~~9. The method of claim 8, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 5.~~

~~10. The method of claim 9, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 5.~~

~~11. The method of claim 10, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 5.~~

~~12. The method of claim 11, wherein the soluble human tissue factor domain comprises SEQ ID NO: 5.~~

~~13. The method of claim 8, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 9.~~

~~14. The method of claim 13, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 9.~~

~~15. The method of claim 14, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 9.~~

~~16. The method of claim 15, wherein the soluble human tissue factor domain comprises SEQ ID NO: 9.~~

~~17. The method of claim 8, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 10.~~

~~18. The method of claim 17, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 10.~~

~~19. The method of claim 18, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 10.~~

~~20. The method of claim 19, wherein the soluble human tissue factor domain comprises SEQ ID NO: 10.~~

21. The method of ~~any one of claims 8-11, 13-15, and 17-19~~, wherein the soluble human tissue factor domain does not comprise one or more of:

a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;

an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;

a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;

an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;

a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;

an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and

a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.

~~22. The method of claim 21, wherein the soluble human tissue factor domain does not comprise any of:~~

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~

~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~

~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~

~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~

~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~

~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~

~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

~~23. The method of any one of claims 1-22, wherein the soluble tissue factor domain is not capable of binding to Factor VIIa.~~

~~24. The method of any one of claims 1-23, wherein the soluble tissue factor domain does not convert inactive Factor X into Factor Xa.~~

~~1025. The method of any one of claims 1-924, wherein the first multi-chain chimeric polypeptide and the second multi-chain chimeric polypeptide do does not stimulate coagulation in a mammal.~~

~~26. The method of any one of claims 1-25, wherein the first chimeric polypeptide and/or the second chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a signal sequence at its N-terminal end.~~

~~27. The method of claim 26, wherein the signal sequence comprises SEQ ID NO: 28.~~

~~28. The method of claim 27, wherein the signal sequence is SEQ ID NO: 28.~~

~~1129. The method of any one of claims 1-1028, wherein the pair of affinity domains in the first multi-chain chimeric polypeptide and/or the second multi-chain chimeric polypeptide is a sushi domain from an alpha chain of human IL-15 receptor (IL15R α) and a soluble IL-15.~~

~~1230. The method of claim 1129, wherein the soluble IL-15 has a D8N or D8A amino acid substitution.~~

~~31. The method of claim 29, wherein the soluble IL-15 comprises a sequence that is 80% identical to SEQ ID NO: 26.~~

~~32. The method of claim 31, wherein the soluble IL-15 comprises a sequence that is 90% identical to SEQ ID NO: 26.~~

~~33. The method of claim 32, wherein the soluble IL-15 comprises a sequence that is 95% identical to SEQ ID NO: 26.~~

~~34. The method of claim 33, wherein the soluble IL-15 comprises SEQ ID NO: 26.~~

~~35. The method of any one of claims 29-34, wherein the sushi domain of IL15R α comprises a sushi domain from human IL15R α .~~

~~36. The method of claim 35, wherein the sushi domain from human IL15R α comprises a sequence that is 80% identical to SEQ ID NO: 24.~~

~~37. The methods of claim 36, wherein the sushi domain from human IL15R α comprises a sequence that is 90% identical to SEQ ID NO: 24.~~

~~38. The method of claim 37, wherein the sushi domain from human IL15R α comprises a sequence that is 95% identical to SEQ ID NO: 24.~~

~~39. The method of claim 38, wherein the sushi domain from human IL15R α comprises SEQ ID NO: 24.~~

~~40. The method of claim 35, wherein the sushi domain from human IL15R α is a mature full length IL15R α .~~

1341. The method of any one of claims 1-1028, wherein the pair of affinity domains in the first multi-chain chimeric polypeptide and/or the second multi-chain chimeric polypeptide is selected from the group consisting of: barnase and barnstar, a

PKA and an AKAP, adapter/docking tag modules based on mutated RNase I fragments, and SNARE modules based on interactions of the proteins syntaxin, synaptotagmin, synaptobrevin, and SNAP25.

1442. The method of any one of claims 1-~~1341~~, wherein the first target-binding domain and the second target-binding domain in the first multi-chain chimeric polypeptide are each independently a soluble IL-15 or a soluble IL-18.

1543. The method of any one of claims 1-1442, wherein the first target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-12, and the second target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-18.

1644. The method of any one of claims 1-1442, wherein the first target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-18, and the second target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-12.

~~45. The method of claim 53, wherein the first target-binding domain in the first multi-chain chimeric polypeptide comprises a soluble IL-18.~~

1746. The method of claim 1645, wherein: the first target-binding domain in the first multi-chain chimeric polypeptide comprises soluble IL-18 is a soluble human IL-18; and

the second target-binding domain in the first multi-chain chimeric polypeptide comprises a soluble human IL-12.

~~47. The method of claim 46, wherein the soluble human IL-18 comprises a sequence at least 80% identical to SEQ ID NO: 20.~~

~~48. The method of claim 47, wherein the soluble human IL-18 comprises a sequence at least 90% identical to SEQ ID NO: 20.~~

~~49. The method of claim 48, wherein the soluble human IL-18 comprises a sequence at least 95% identical to SEQ ID NO: 20.~~

~~50. The method of claim 49, wherein the soluble human IL-18 comprises a sequence of SEQ ID NO: 20.~~

~~51. The method of any one of claims 44-50, wherein the second target binding domain in the first multi-chain chimeric polypeptide comprises a soluble IL-12.~~

~~52. The method of claim 51, wherein the soluble IL-12 is a soluble human IL-12.~~

~~53. The method of claim 52, wherein the soluble human IL-12 comprises a sequence of soluble human IL-12 β (p40) and a sequence of soluble human IL-12 α (p35).~~

~~54. The method of claim 53, wherein the soluble human IL-15 further comprises a linker sequence between the sequence of soluble IL-12 β (p40) and the sequence of soluble human IL-12 α (p35).~~

~~55. The method of claim 54, wherein the linker sequence comprises SEQ ID NO: 11.~~

~~56. The method of any one of claims 53-55, wherein the sequence of soluble human IL-12 β (p40) comprises a sequence that is at least 80% identical to SEQ ID NO: 14.~~

~~57. The method of claim 56, wherein the sequence of soluble human IL-12 β (p40) comprises a sequence that is at least 90% identical to SEQ ID NO: 14.~~

~~58. The method of claim 57, wherein the sequence of soluble human IL-12 β (p40) comprises a sequence that is at least 95% identical to SEQ ID NO: 14.~~

~~59. The method of claim 58, wherein the sequence of soluble human IL-12 β (p40) comprises SEQ ID NO: 14.~~

~~60. The method of any one of claims 53-59, wherein the sequence of soluble human IL-12 α (p35) comprises a sequence that is at least 80% identical to SEQ ID NO: 16.~~

~~61. The method of claim 60, wherein the sequence of soluble human IL-12 α (p35) comprises a sequence that is at least 90% identical to SEQ ID NO: 16.~~

~~62. The method claim 61, wherein the sequence of soluble human IL-12 α (p35) comprises a sequence that is at least 95% identical to SEQ ID NO: 16.~~

~~63. The method of claim 62, wherein the sequence of soluble human IL-12 α (p35) comprises SEQ ID NO: 16.~~

1864. The method of claim 1, wherein:

the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to
YFGKLESKLSVIRNLNDQVLFDQGNRPLFEDMTDSDCRDNAPRTIFIISMYKD
SQPRGMAVTISVKCEKISTLSCENKIISFKEMNPPDNIKDTKSDIIFQRSVPGH
DNKMQFESSSYEGYFLACEKERDLFKLILKKEDELGDRSIMFTVQNEGSGTTN
TVAAYNLTWKSTNFKTILEWEPKPVNQVYTVQISTKSGDWKSKCFYTTDTEC
DLTDEIVKDVKQTYLARVFSYPAGNVESTGSAGEPLYENSPEFTPYLETNLGQ
PTIQSFEQVGTKVNVTVEDERTLVRRNNTFLSLRDVFGKDLIYTLYYWKSSSS
GKKTAKTNTNEFLIDVDKGENYCFVSQAVIPSRTVNRKSTDSPVECMGQKEG
EFRENWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQV
ISLESGDASIHDVTENLIILANNSLSSNGNVTESGCKECEEELEEKNIKEFLQSFV
HIVQMFINTS (SEQ ID NO: 63); and

the second chimeric polypeptide comprises a sequence that is at least 80% identical to
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGK
TLTIQVKEFGDAGQYTCHKGGEVLSHSLLLHKKEDGIWSTDILKDQKEPKN

KTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAE
RVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIR
DIKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKR
EKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCSGGGGSGG
GGSGGGGSRNLPVATPDPGMFPCLHHSQNLLRAVSNMLQKARQTLEFYPCTS
EEIDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRKTSFMM
ALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALN
FNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNASITCPPPM
SVEHADIWVKSYSLSYRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTPP
SLKCIR (SEQ ID NO: 65).

~~65. The method of claim 64, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 63.~~

~~66. The method of claim 65, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 63.~~

~~67. The method of claim 66, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises SEQ ID NO: 63.~~

~~68. The method of claim 67, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises~~
MKWVTFISLLFLSSAYSIFGKLESKLSVIRNLNDQVLFIDQGNRPLFEDMTD
SDCRDNAPRTIFHSMYKDSQPRGMAVTISVKCEKISTLSCENKHSFKEMNPPD
NIKDTKSDIHFQRSVPGHDKMQFESSSYEGYFLACEKERDLFKLILKKEDEL
GDRSIMFTVQNEDSGTTNTVAAYNLTWKSTNFKTILEWEPKPVNQVYTVQIS
TKSGDWKSKCFYTTDTECDLTDEIVKDVKQTYLARVFSYPAGNVESTGSAGE
PLYENSPEFTPYLETNLGQPTIQSFEQVGTKVNVTVEDERTLVRRNNTFLSLR
DVFGKDLIYTLYYWKSSSSGKKTAKTNTNEFLIDVDKGENYCFSVQAVIPSRT
VNRKSTDSPVECMGQEKGEFRENWVNVISDLKKIEDLIQSMHIDATLYTESD

VHPSCKVTAMKCFLLLELQVISLESGDASHDTVENLILANNSLSSNGNVTESG
CKECEEELEEKNIKEFLQSFVHIVQMFINTS (SEQ ID NO: 64).

69. The method of any one of claims 1 and 64-68, wherein the second
chimeric polypeptide comprises a sequence that is at least 80% identical to
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGK
TLTIQVKEFGDAGQYTCHKGGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKN
KTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAE
RVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIR
DHKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKR
EKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCSGGGGGSGG
GGSGGGGSRNLPVATPDPGMFPCLLHHSQNLLRAVSNMLQKARQTLEFYPTCS
EEIDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRKTSFMM
ALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALN
FNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNASITCPPPM
SVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSSLTECVLNKATNVAHWTP
SLKCIR (SEQ ID NO: 65).

70. The method of claim 69, wherein the second chimeric polypeptide
comprises a sequence that is at least 90% identical to SEQ ID NO: 65.

71. The method of claim 70, wherein the second chimeric polypeptide
comprises a sequence that is at least 95% identical to SEQ ID NO: 65.

72. The method of claim 71, wherein the second chimeric polypeptide
comprises SEQ ID NO: 65.

73. The method of claim 72, wherein the second chimeric polypeptide
comprises
MKWVTFISLLFLSSAYSIWELKKDVYVVELDWYPDAPGEMVVLTCDTPEED
GITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHSLLLLHKKE
DGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRG
SSDPQGVTCGAATLSAERVGRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVD

AVHKLKYENYTSSFFIRDHKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPH
SYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSS
WSEWASVPCSGGGGSGGGGSGGGGSRNLPVATPDPGMFPCLLHHSQNLLRAV
SNMLQKARQTLEFPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFL
DQNMLAVIDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTH
DRVMSYLNASITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLT
ECVLNKATNVAHWTPSLKCIR (SEQ ID NO: 66).

1974. The method of any one of claims 1-1873, wherein the first target-binding domain and the linker domain in the first chimeric polypeptide in the second multi-chain chimeric polypeptide directly abut each other in the first chimeric polypeptide.

2075. The method of any one of claims 1-1873, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a linker sequence between the first target-binding domain and the linker domain in the first chimeric polypeptide.

2176. The method of any one of claims 1-2075, wherein the linker domain and the first domain of the pair of affinity domains directly abut each other in the first chimeric polypeptide in the second multi-chain chimeric polypeptide.

2277. The method of any one of claims 1-2075, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a linker sequence between the linker domain and the first domain of the pair of affinity domains in the first chimeric polypeptide.

2378. The method of any one of claims 1-2277, wherein the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide of the second multi-chain chimeric polypeptide directly abut each other in the second chimeric polypeptide.

~~2479.~~ The method of any one of claims 1-~~2277~~, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a linker sequence between the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide.

~~80. The method of any one of claims 1-79, wherein the linker domain is a soluble tissue factor domain.~~

~~81. The method of claim 80, wherein the soluble tissue factor domain is a soluble human tissue factor domain.~~

~~82. The method of claim 81, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 5.~~

~~83. The method of claim 82, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 5.~~

~~84. The method of claim 83, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 5.~~

~~85. The method of claim 84, wherein the soluble human tissue factor domain comprises SEQ ID NO: 5.~~

~~86. The method of claim 81, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 9.~~

~~87. The method of claim 86, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 9.~~

~~88. The method of claim 87, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 9.~~

~~89. The method of claim 88, wherein the soluble human tissue factor domain comprises SEQ ID NO: 9.~~

~~90. The method of claim 81, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 10.~~

~~91. The method of claim 90, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 10.~~

~~92. The method of claim 91, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 10.~~

~~93. The method of claim 92, wherein the soluble human tissue factor domain comprises SEQ ID NO: 10.~~

~~94. The method of any one of claims 82-84, 86-88, and 90-92, wherein the soluble human tissue factor domain does not comprise one or more of:~~

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~

~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~

~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~

~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~

~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~

~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~

~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

~~95. The method of claim 94, wherein the soluble human tissue factor domain does not comprise any of:~~

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~

~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~

~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~

~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~

~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~

~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~

~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

~~96. The method of any one of claims 81-95, wherein the soluble tissue factor domain is not capable of binding to Factor VIIa.~~

~~97. The method of any one of claims 81-96, wherein the soluble tissue factor domain does not convert inactive Factor X into Factor Xa.~~

~~98. The method of any one of claims 81-97, wherein the second multi-chain chimeric polypeptide does not stimulate coagulation in a mammal.~~

~~99. The method of any one of claims 1-98, wherein the first chimeric polypeptide and/or the second chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a signal sequence at its N-terminal end.~~

~~100. The method of claim 99, wherein the signal sequence comprises SEQ ID NO: 28.~~

~~101. The method of claim 100, wherein the signal sequence is SEQ ID NO: 28.~~

~~102. The method of any one of claims 1-101, wherein the pair of affinity domains in the second multi-chain chimeric polypeptide is a sushi domain from an alpha chain of human IL-15 receptor (IL15R α) and a soluble IL-15.~~

~~103. The method of claim 102, wherein the soluble IL-15 has a D8N or D8A amino acid substitution.~~

~~104. The method of claim 102, wherein the soluble IL-15 comprises a sequence that is 80% identical to SEQ ID NO: 26.~~

~~105. The method of claim 104, wherein the soluble IL-15 comprises a sequence that is 90% identical to SEQ ID NO: 26.~~

~~106. The method of claim 105, wherein the soluble IL-15 comprises a sequence that is 95% identical to SEQ ID NO: 26.~~

~~107. The method of claim 106, wherein the soluble IL-15 comprises SEQ ID NO: 26.~~

~~108. The method of any one of claims 102-107, wherein the sushi domain of IL15R α comprises a sushi domain from human IL15R α .~~

~~109. The method of claim 108, wherein the sushi domain from human IL15R α comprises a sequence that is 80% identical to SEQ ID NO: 24.~~

~~110. The methods of claim 109, wherein the sushi domain from human IL15R α comprises a sequence that is 90% identical to SEQ ID NO: 24.~~

~~111. The method of claim 110, wherein the sushi domain from human IL15R α comprises a sequence that is 95% identical to SEQ ID NO: 24.~~

~~112. The method of claim 111, wherein the sushi domain from human IL15R α comprises SEQ ID NO: 24.~~

~~113. The method of claim 108, wherein the sushi domain from human IL15R α is a mature full-length IL15R α .~~

~~114. The method of any one of claims 1-101, wherein the pair of affinity domains in the second multi-chain chimeric polypeptide is selected from the group consisting of: barnase and barnstar, a PKA and an AKAP, adapter/docking tag modules based on mutated RNase I fragments, and SNARE modules based on interactions of the proteins syntaxin, synaptotagmin, synaptobrevin, and SNAP25.~~

2115. The method of any one of claims 1-~~2114~~, wherein the first target-binding domain and the second target-binding domain in the second multi-chain chimeric polypeptide are each independently a soluble IL-7 or a soluble IL-21.

2116. The method of any one of claims 1-~~2115~~, wherein the first target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-21, and the second target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-7.

2117. The method of any one of claims 1-~~2115~~, wherein the first target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-7, and the second target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-21.

~~118. The method of claim 117, wherein the first target binding domain in the second multi-chain chimeric polypeptide comprises a soluble IL-21.~~

28119. The method of claim ~~27118~~, wherein:
the first target-binding domain in the second multi-chain chimeric polypeptide comprises soluble IL-21 is a soluble human IL-~~721~~; and
the second target-binding domain in the second multi-chain chimeric polypeptide comprises a soluble human IL-21.

~~120. The method of claim 119, wherein the soluble human IL-21 comprises a sequence at least 80% identical to SEQ ID NO: 22.~~

~~121. The method of claim 120, wherein the soluble human IL-21 comprises a sequence at least 90% identical to SEQ ID NO: 22.~~

~~122. The method of claim 121, wherein the soluble human IL-21 comprises a sequence at least 95% identical to SEQ ID NO: 22.~~

~~123. The method of claim 122, wherein the soluble human IL-21 comprises a sequence of SEQ ID NO: 22.~~

~~124. The method of any one of claims 117-123, wherein the second target-binding domain comprises a soluble IL-7.~~

~~125. The method of claim 124, wherein the soluble IL-7 is a soluble human IL-7.~~

~~126. The method of claim 125, wherein the soluble human IL-7 comprises a sequence at least 80% identical to SEQ ID NO: 23.~~

~~127. The method of claim 126, wherein the soluble human IL-7 comprises a sequence at least 90% identical to SEQ ID NO: 23.~~

~~128. The method of claim 127, wherein the soluble human IL-7 comprises a sequence at least 95% identical to SEQ ID NO: 23.~~

~~129. The method of claim 128, wherein the soluble human IL-7 comprises a sequence of SEQ ID NO: 23.~~

~~29130. The method of claim 1, wherein:~~

the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to
DCDIEGKDGKQYESVLMVSIQQLDSMKEIGSNCLNNEFNFFKRHICDANKE

GMFLFRAARKLRQFLKMNSTGDFDLHLLKVSEGTTILLNCTGQVKGRKPAAL
GEAQPTKSLEENKSLKEQKKLNDLCFLKRLLQEIKTCWNKILMGTKEHSGTT
NTVAAYNLTWKSTNFKTILEWEPKPVNQVYTVQISTKSGDWKSKCFYTTDTE
CDLTDEIVKDVKQTYLARVFSYPAGNVESTGSAGEPLYENSPEFTPYLETNLG
OPTIQSFEQVGTKVNVTVEDERTLVRRNNTFLSLRDVFGKDLYTLYYWKSSS
SGKKTAKTNTNEFLIDVDKGENYCFSVQAVIPSRTVNRKSTDSPVECMGQEK
GEFRENWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQ
VISLESGDASIHTVENLIILANNSLSSNGNVTESGCKECEEELEEKNIKEFLQSF
VHIVQMFINTS (SEQ ID NO: 67); and

the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to
QGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQK
AQLKSANTGNNERIINVSIIKKLRKPPSTNAGRRQKHRLTCPSCDSYEKKPPK
EFLERFKSLQKMIHQHLSSRTHGSEDSITCPPPMSVEHADIWVKSYSLSYRER
YICNSGFKRKAGTSSLTECVLNKATNVAHWTPSLKCIR (SEQ ID NO: 69).

~~131. The method of claim 130, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 67.~~

~~132. The method of claim 131, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 67.~~

~~133. The method of claim 132, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 67.~~

~~134. The method of claim 133, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises~~
~~MKWVTFISLLFLFSSAYSDCDIEGKDQKQYESVLMVSDQLLDSMKEIGSNCL~~
~~NNEFNFFKRHICDANKEGMFLFRAARKLRQFLKMNSTGDFDLHLLKVSEGTT~~
~~ILLNCTGQVKGRKPAALGEAQPTKSLEENKSLKEQKKLNDLCFLKRLLQEIKT~~
~~CWNKILMGTKEHSGTTNTVAAYNLTWKSTNFKTILEWEPKPVNQVYTVQIST~~
~~KSGDWKSKCFYTTDTECDLTDEIVKDVKQTYLARVFSYPAGNVESTGSAGEP~~

LYENSPEFTPYLETNLGQPTIQSFEQVGTKVNVTVEDERTLVRRNNTFLSLRD
VFGKDLIYTLYYWKSSSSGKKTAKTNTNEFLIDVDKGENYCFQSVQAVIPSRTV
NRKSTDSPVECMGQEKGEFRENWVNVISDLKKIEDLIQSMHIDATLYTESDV
HPSCCKVTAMKCFLELQVISLESQDASHDTVENLHLANNSSNGNVTESGC
KECEELEEKNIKEFLQSFVHIVQMFINTS (SEQ ID NO: 68).

135. The method of any one of claims 1 and 130-134, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to

QGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQK
AQLKSANTGNNERIINVSIKKLKRKPPSTNAGRRQKHRLTCPSCDSYEKKPPK
EFLERFKSLQKMIHQHLSSRTHGSEDSITCPPPMSVEHADIWVKSYSLYSRER
YICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR (SEQ ID NO: 69).

136. The method of claim 135, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 69.

137. The method of claim 136, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 69.

138. The method of claim 137, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 69.

139. The method of claim 138, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises

MKWVTFISLLFLSSAYSQGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAP
EDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSIKKLKRKPPSTNAGRRQK
HRLTCPSCDSYEKKPPKEFLERFKSLQKMIHQHLSSRTHGSEDSITCPPPMSV
EHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSL
KCIR (SEQ ID NO: 70).

~~314~~40. The method of claim 1, wherein:

the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to

QGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQK
AQLKSANTGNNERIINVSIIKKLKRKPPSTNAGRRQKHRLTCPSCDSYEKKPPK
EFLERFKSLLQKMIHQHLSSRTHGSEDSSGTTNTVAAYNLTWKSTNFKTILEW
EPKPVNQVYTVQISTKSGDWKSKCFYTTDTECDLTDEIVKDVKQTYLARVFS
YPAGNVESTGSAGEPLYENSPEFTPYLETNLGQPTIQSFEQVGTKVNVTVDEDE
RTLVRNNTFLSLRDVFGKDLIYTLYYWKSSSSGKKTAKTNTNEFLIDVDKG
ENYCFSVQAVIPSRTVNRKSTDSPVECMGQEKGEFRENWVNVISDLKKIEDLI
QSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLES GDASIHD TVENLIILA
NNSLSSNGNVTESGCKECELEEKNIKEFLQSFVHIVQMFINTS (SEQ ID NO:
71); and

the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to
DCDIEGKD GKQYESVLMV SIDQLLDSMKEIGSNCLNNEFNFFKRHICDANKE
GMFLFRAARKLRQFLKMNSTGDFDLHLLKVSEGTTILLNCTGQVKGRKPAAL
GEAQPTKSLEENKSLKEQKKLNDLCFLKRLQEIKTCWNKILMGTKEHITCPP
PMSVEHADIWVKSYSLSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWT
TPSLKCIR (SEQ ID NO: 73).

~~141. The method of claim 140, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 71.~~

~~142. The method of claim 141, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 71.~~

~~143. The method of claim 142, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 71.~~

~~144. The method of claim 143, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises~~
MGVKVLFALICIAVAEAQGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAP
EDVETNCEWSAFSCFQKAQLKSANTGNNERIINVSIKKLKRKPPSTNAGRRQK
HRLTCPSCDSYEKKPPKEFLERFKSLLQKMIHQHLSSRTHGSEDSSGTTNTVA
AYNLTWKSTNFKTILEWEPKPVNQVYTVQISTKSGDWKSKCFYTTDTECDLT
DEIVKDVKQTYLARVFSYPAGNVESTGSAGEPLYENSPEFTPYLETNLGQPTI
QSFEQVGTKVNVTVEDERTLVRRNNTFLSLRDVFGKDLIYTLYYWKSSSSGK
KTAKTNTNEFLIDVDKGENYCFSVQAVIPSRTVNRKSTDSPVECMGQEKGEF
RENWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLEELQVIS
LESGDASHDTVENLHILANNSLSSNGNVTESGCKECELEEKNIKEFLQSFVHI
VQMFINTS (SEQ ID NO: 72).

~~145. The method of any one of claims 1 and 140-144, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to~~
DCDIEGKDGKQYESVLMVSIDQLLDSMKEIGSNCLNNEFNFFKRHICDANKE
GMFLFRAARKLRQFLKMNSTGDFDLHLLKVSEGTTILLNCTGQVKGRKPAAL
GEAQPTKSLEENKSLKEQKKLNDLCFLKRLLQEIKTCWNKILMGTKEHITCPP
PMSVEHADIWVKSYSLSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWT
TPSLKCIR (SEQ ID NO: 73).

~~146. The method of claim 145, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 73.~~

~~147. The method of claim 146, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 73.~~

~~148. The method of claim 147, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 73.~~

~~149. The method of claim 148, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises~~
MGVKVLFALICIAVAEADCDIEGKDQKQYESVLMVSIQQLDLSMKEIGSNCL
NNEFNFFKRHICDANKEGMFLFRAARKLRQFLKMNSTGDFDLHLLKVSEGTT
ILLNCTGQVKGRKPAALGEAQPTKSLEENKSLKEQKKLNDLCFLKRLLEIQT
CWNKILMGTKEHITCPPPMSVEHADIWVKSYSLSRERYICNSGFKRKAGTSS
LTECVLNKATNVAHWTTPSLKCIR (SEQ ID NO: 74).

31450. The method of any one of claims 1-~~30149~~, wherein the IgG1 antibody construct is a monoclonal IgG1 antibody, where both antigen-binding domains in the monoclonal IgG1 antibody bind specifically to the linker domain.

~~151. The method of any one of claims 1-149, wherein the IgG1 antibody construct is a bispecific IgG1 antibody, where one of the two antigen-binding domains in the bispecific IgG1 antibody binds specifically to the linker domain.~~

31452. The method of any one of claims 1-~~3151~~, wherein the first period of time is about 15 minutes to about 4 hours, and the second period of time is about 1 day to about 30 days.

~~153. The method of claim 152, wherein the first period of time is about 30 minutes to about 3.5 hours.~~

~~154. The method of claim 153, wherein the first period of time is about 1 hour to about 3.5 hours.~~

~~155. The method of claim 154, wherein the first period of time is about 2 hours to about 3.5 hours.~~

~~156. The method of any one of claims 1-155, wherein the liquid culture medium in step (a) and/or step (b) is a serum-containing liquid culture medium.~~

~~157. The method of any one of claims 1-156, wherein the NK cells are in the liquid culture medium in step (a) at a density of about 4.0×10^7 cells/mL to about 1.5×10^8 cells/mL.~~

~~158. The method of claim 157, wherein the NK cells are in the liquid culture medium in step (a) at a density of about 5.0×10^7 cells/mL to about 2.0×10^8 cells/mL.~~

~~159. The method of any one of claims 1-158, wherein the second period of time is about 1 day to about 30 days.~~

~~160. The method of claim 159, wherein the second period of time is about 7 days to about 30 days.~~

~~161. The method of claim 160, wherein the second period of time is about 14 days to about 21 days.~~

~~33162. The method of any one of claims 1-32161, wherein the liquid culture medium in step (b) comprises the second multi-chain chimeric polypeptide and the IgG1 antibody construct at a molar ratio of about 0.5:1 to about 2:1.~~

~~163. The method of claim 162, wherein the liquid culture medium in step (b) comprises the second multi-chain chimeric polypeptide and the IgG1 antibody construct at a molar ratio of about 0.8:1 to about 1.2:1.~~

~~164. The method of any one of claims 1-163, wherein the NK cells are in the liquid culture medium in step (b) are maintained at a density of about 0.5×10^6 cells/mL to about 2.0×10^6 cells/mL.~~

~~165. The method of claim 164, wherein the NK cells are in the liquid culture medium in step (b) are maintained at a density of about 1.0×10^6 cells/mL to about 2.0×10^6 cells/mL.~~

~~34166.~~ The method of any one of claims 1-~~33165~~, wherein the NK cell was previously obtained from a subject.

~~167.~~ The method of any one of claims 1-165, wherein the NK cell was previously obtained from umbilical cord blood.

~~168.~~ The method of any one of claims 1-165, wherein the NK cell was previously obtained from an induced pluripotent stem cell.

~~35169.~~ The method of claim ~~166 or 167~~~~34~~, wherein ~~the method further comprises obtaining~~ the NK cell is to be obtained from the subject prior to step (a).

~~36170.~~ The method of any one of claims 1-~~35169~~, wherein the NK cell has previously been genetically modified to express a chimeric antigen receptor or a recombinant T-cell receptor.

~~171.~~ The method of any one of claims 1-169, wherein the method further comprises, between step (a) and step (b), introducing into the NK cell a nucleic acid encoding a chimeric antigen receptor or a recombinant T-cell receptor.

~~172.~~ The method of any one of claims 1-169, wherein the method further comprises, prior to step (a), introducing into the NK cell a nucleic acid encoding a chimeric antigen receptor or a recombinant T-cell receptor.

~~173.~~ The method of any one of claims 1-169, wherein the method further comprises, during step (b), introducing into the NK cell a nucleic acid encoding a chimeric antigen receptor or a recombinant T-cell receptor.

~~37174.~~ The method of any one of claims 1-~~36173~~, wherein the method further comprises, after step (b), isolating the NK cell.

~~175.~~ The method of any one of claims 1-174, wherein after step (b), the NK cell has an increased level of expression or secretion of one or more proteins selected

from the group consisting of: TNF- α , IFN- γ , granzyme A, granzyme B, perforin, 2B4, CD8, CD11a, CD16, CD25, CD27, CD48, CD49d, CD54, CD56, CD58, CD62L, CD69, CD70, CD94, CD137, CD158a, CD158b, CD158e, CD178, CD226, CD253, NKG2C, NKG2D, LIR-1, LILR-B1, KIR2DL1, KIR3DL1, KIR2DL2, KIR2DL3, CXCR3, NKp30, NKp44, NKp46, NKG2D, DNAM-1, TRAIL, FasL, CXCR3, CXCR4, LTB, MX1, BAX, TNF- α , and IFN- γ as compared to the level of expression or secretion of the one or more proteins prior to step (a).

~~38176.~~ The method of any one of claims 1-~~3177~~, wherein the ~~method further comprises,~~ NK cell is to be administered to a subject in need thereof, after the contacting step, ~~administering the NK cell to a subject in need thereof.~~

~~177.~~ The method of claim ~~176~~, wherein the subject has been identified or diagnosed as having an age-related disease or condition.

~~178.~~ The method of claim ~~177~~, wherein the age-related disease or condition is selected from the group consisting of: Alzheimer's disease, aneurysm, cystic fibrosis, fibrosis in pancreatitis, glaucoma, hypertension, idiopathic pulmonary fibrosis, inflammatory bowel disease, intervertebral disc degeneration, macular degeneration, osteoarthritis, type 2 diabetes mellitus, adipose atrophy, lipodystrophy, atherosclerosis, cataracts, COPD, idiopathic pulmonary fibrosis, kidney transplant failure, liver fibrosis, loss of bone mass, myocardial infarction, sarcopenia, wound healing, alopecia, cardiomyocyte hypertrophy, osteoarthritis, Parkinson's disease, age-associated loss of lung tissue elasticity, macular degeneration, cachexia, glomerulosclerosis, liver cirrhosis, NAFLD, osteoporosis, amyotrophic lateral sclerosis, Huntington's disease, spinocerebellar ataxia, multiple sclerosis, and renal dysfunction.

~~179.~~ The method of claim ~~176~~, wherein the subject has been identified or diagnosed as having a cancer.

~~180.~~ The method of claim ~~179~~, wherein the cancer is selected from the group consisting of: solid tumor, hematological tumor, sarcoma, osteosarcoma,

~~glioblastoma, neuroblastoma, melanoma, rhabdomyosarcoma, Ewing sarcoma, osteosarcoma, B-cell neoplasms, multiple myeloma, B-cell lymphoma, B-cell non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma, retinoblastoma, stomach cancer, urothelial carcinoma, lung cancer, renal cell carcinoma, gastric and esophageal cancer, pancreatic cancer, prostate cancer, breast cancer, colorectal cancer, ovarian cancer, non-small cell lung carcinoma, squamous cell head and neck carcinoma, endometrial cancer, cervical cancer, liver cancer, and hepatocellular carcinoma.~~

~~181. The method of claim 176, wherein the subject has been diagnosed or identified as having an infectious disease.~~

~~182. The method of claim 181, wherein the infectious disease is infection with human immunodeficiency virus, cytomegalovirus, adenovirus, coronavirus, rhinovirus, rotavirus, smallpox, herpes simplex virus, hepatitis B virus, hepatitis A virus, and hepatitis C virus, papillomavirus, and influenza virus.~~

39183. An activated NK cell produced by the method of any one of claims 1-~~38182~~.

40184. A pharmaceutical composition comprising the activated NK cell of claim 39183.

41185. A kit comprising a pharmaceutical composition comprising the activated NK cell of claim 39183.

42186. Use of A method of killing a cancer cell, an infected cell, or a senescent cell in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the activated NK cell of claim 39183 or the pharmaceutical composition of claim 40184 in the manufacture of a medicament

for killing a cancer cell, an infected cell, or a senescent cell in a subject in need thereof.

~~187. The method of claim 186, wherein the subject has been identified or diagnosed as having a cancer.~~

~~188. The method of claim 187, wherein the cancer is selected from the group consisting of: solid tumor, hematological tumor, sarcoma, osteosarcoma, glioblastoma, neuroblastoma, melanoma, rhabdomyosarcoma, Ewing sarcoma, osteosarcoma, B-cell neoplasms, multiple myeloma, B-cell lymphoma, B-cell non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma, retinoblastoma, stomach cancer, urothelial carcinoma, lung cancer, renal cell carcinoma, gastric and esophageal cancer, pancreatic cancer, prostate cancer, breast cancer, colorectal cancer, ovarian cancer, non-small cell lung carcinoma, squamous cell head and neck carcinoma, endometrial cancer, cervical cancer, liver cancer, and hepatocellular carcinoma.~~

~~189. The method of claim 186, wherein the subject has been identified or diagnosed as having an aging-related disease or condition.~~

~~190. The method of claim 189, wherein the aging-related disease or condition is selected from the group consisting of: Alzheimer's disease, aneurysm, cystic fibrosis, fibrosis in pancreatitis, glaucoma, hypertension, idiopathic pulmonary fibrosis, inflammatory bowel disease, intervertebral disc degeneration, macular degeneration, osteoarthritis, type 2 diabetes mellitus, adipose atrophy, lipodystrophy, atherosclerosis, cataracts, COPD, idiopathic pulmonary fibrosis, kidney transplant failure, liver fibrosis, loss of bone mass, myocardial infarction, sarcopenia, wound healing, alopecia, cardiomyocyte hypertrophy, osteoarthritis, Parkinson's disease, age-associated loss of lung tissue elasticity, macular degeneration, cachexia, glomerulosclerosis, liver cirrhosis, NAFLD, osteoporosis, amyotrophic lateral~~

sclerosis, Huntington's disease, spinocerebellar ataxia, multiple sclerosis, and renal dysfunction.

~~191. The method of claim 186, wherein the subject has been diagnosed or identified as having an infectious disease.~~

~~192. The method of claim 191, wherein the infectious disease is infection with human immunodeficiency virus, cytomegalovirus, adenovirus, coronavirus, rhinovirus, rotavirus, smallpox, herpes simplex virus, hepatitis B virus, hepatitis A virus, and hepatitis C virus, papillomavirus, and influenza virus.~~

~~43193. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount Use of the activated NK cell or the activated T cell of claim ~~39183~~ or the pharmaceutical composition of claim ~~40184~~ in the manufacture of a medicament for treating a subject in need thereof.~~

~~194. The method of claim 193, wherein the subject has been identified or diagnosed as having a cancer.~~

~~195. The method of claim 194, wherein the cancer is selected from the group consisting of: solid tumor, hematological tumor, sarcoma, osteosarcoma, glioblastoma, neuroblastoma, melanoma, rhabdomyosarcoma, Ewing sarcoma, osteosarcoma, B-cell neoplasms, multiple myeloma, B-cell lymphoma, B-cell non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma, retinoblastoma, stomach cancer, urothelial carcinoma, lung cancer, renal cell carcinoma, gastric and esophageal cancer, pancreatic cancer, prostate cancer, breast cancer, colorectal cancer, ovarian cancer, non-small cell lung carcinoma, squamous cell head and neck carcinoma, endometrial cancer, cervical cancer, liver cancer, and hepatocellular carcinoma.~~

~~196. The method of claim 193, wherein the subject has been identified or diagnosed as having an aging-related disease or condition.~~

~~197. The method of claim 196, wherein the aging-related disease or condition is selected from the group consisting of: Alzheimer's disease, aneurysm, cystic fibrosis, fibrosis in pancreatitis, glaucoma, hypertension, idiopathic pulmonary fibrosis, inflammatory bowel disease, intervertebral disc degeneration, macular degeneration, osteoarthritis, type 2 diabetes mellitus, adipose atrophy, lipodystrophy, atherosclerosis, cataracts, COPD, idiopathic pulmonary fibrosis, kidney transplant failure, liver fibrosis, loss of bone mass, myocardial infarction, sarcopenia, wound healing, alopecia, cardiomyocyte hypertrophy, osteoarthritis, Parkinson's disease, age-associated loss of lung tissue elasticity, macular degeneration, cachexia, glomerulosclerosis, liver cirrhosis, NAFLD, osteoporosis, amyotrophic lateral sclerosis, Huntington's disease, spinocerebellar ataxia, multiple sclerosis, and renal dysfunction.~~

~~198. The method of claim 197, wherein the subject has been diagnosed or identified as having an infectious disease.~~

~~199. The method of claim 198, wherein the infectious disease is infection with human immunodeficiency virus, cytomegalovirus, adenovirus, coronavirus, rhinovirus, rotavirus, smallpox, herpes simplex virus, hepatitis B virus, hepatitis A virus, and hepatitis C virus, papillomavirus, and influenza virus.~~

44200. A kit comprising:

(a) a first multi-chain chimeric polypeptide comprises:

a first chimeric polypeptide comprising a first target-binding domain, a soluble tissue factor domain, and a first domain of a pair of affinity domains, and

a second chimeric polypeptide comprising a second domain of a pair of affinity domains and a second target-binding domain,

wherein the first chimeric polypeptide and the second chimeric polypeptide in the first multi-chain chimeric polypeptide associate through

the binding of the first domain and the second domain of the pair of affinity domains in the first multi-chain chimeric polypeptide, and the first target-binding domain and the second target-binding domain in the first multi-chain chimeric polypeptide each independently bind specifically to a receptor of IL-18 or a receptor of IL-12;

(b) a second multi-chain chimeric polypeptide comprises:

a first chimeric polypeptide comprising a first target-binding domain, a linker domain, a first domain of a pair of affinity domains, and

a second chimeric polypeptide comprising a second domain of a pair of affinity domains, and a second target-binding domain,

wherein the first chimeric polypeptide and the second chimeric polypeptide in the second multi-chain chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains in the second multi-chain chimeric polypeptide; and the first target-binding domain and the second target-binding domain in the second multi-chain chimeric polypeptide each independently bind specifically to a receptor for IL-7 or a receptor for IL-21; and

(c) an IgG1 antibody that comprises at least one antigen-binding domain that binds specifically to the linker domain.

~~201. The kit of claim 200, wherein the first target binding domain and the soluble tissue factor domain directly abut each other in the first chimeric polypeptide in the first multi-chain chimeric polypeptide.~~

~~202. The kit of claim 200, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a linker sequence between the first target binding domain and the soluble tissue factor domain in the first chimeric polypeptide.~~

~~203. The kit of any one of claims 200-202, wherein the soluble tissue factor domain and the first domain of the pair of affinity domains in the first chimeric polypeptide in the first multi-chain chimeric polypeptide directly abut each other in the first chimeric polypeptide.~~

~~204. The kit of any one of claims 200-202, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the first domain of the pair of affinity domains in the first chimeric polypeptide.~~

~~205. The kit of any one of claims 200-204, wherein the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide in the first multi-chain chimeric polypeptide directly abut each other in the second chimeric polypeptide.~~

~~206. The kit of any one of claims 200-204, wherein the second chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a linker sequence between the second domain of the pair of affinity domains and the second target-binding domain in the second chimeric polypeptide.~~

~~207. The kit of any one of claims 200-206, wherein the soluble tissue factor domain is a soluble human tissue factor domain.~~

~~208. The kit of claim 207, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 5.~~

~~209. The kit of claim 208, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 5.~~

~~210. The kit of claim 209, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 5.~~

~~211. The kit of claim 210, wherein the soluble human tissue factor domain comprises SEQ ID NO: 5.~~

~~212. The kit of claim 207, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 9.~~

~~213. The kit of claim 212, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 9.~~

~~214. The kit of claim 213, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 9.~~

~~215. The kit of claim 214, wherein the soluble human tissue factor domain comprises SEQ ID NO: 9.~~

~~216. The kit of claim 207, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 10.~~

~~217. The kit of claim 216, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 10.~~

~~218. The kit of claim 217, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 10.~~

~~219. The kit of claim 218, wherein the soluble human tissue factor domain comprises SEQ ID NO: 10.~~

~~220. The kit of any one of claims 207-210, 212-214, and 216-218, wherein the soluble human tissue factor domain does not comprise one or more of:~~

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~

~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~

~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~

~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~

~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~

~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~

~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

~~221. The kit of claim 220, wherein the soluble human tissue factor domain does not comprise any of:~~

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~

~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~

~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~

~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~

~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~

~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~

~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

~~222. The kit of any one of claims 200-221, wherein the soluble tissue factor domain is not capable of binding to Factor VIIa.~~

~~223. The kit of any one of claims 200-222, wherein the soluble tissue factor domain does not convert inactive Factor X into Factor Xa.~~

~~224. The kit of any one of claims 200-223, wherein the first multi-chain chimeric polypeptide does not stimulate coagulation in a mammal.~~

~~225. The kit of any one of claims 200-224, wherein the first chimeric polypeptide and/or the second chimeric polypeptide in the first multi-chain chimeric polypeptide further comprises a signal sequence at its N-terminal end.~~

~~226. The kit of claim 225, wherein the signal sequence comprises SEQ ID NO: 28.~~

~~227. The kit of claim 226, wherein the signal sequence is SEQ ID NO: 28.~~

~~228. The kit of any one of claims 200-227, wherein the pair of affinity domains in the first multi-chain chimeric polypeptide is a sushi domain from an alpha chain of human IL-15 receptor (IL15R α) and a soluble IL-15.~~

~~229. The kit of claim 228, wherein the soluble IL-15 has a D8N or D8A amino acid substitution.~~

~~230. The kit of claim 228, wherein the soluble IL-15 comprises a sequence that is 80% identical to SEQ ID NO: 26.~~

~~231. The kit of claim 230, wherein the soluble IL-15 comprises a sequence that is 90% identical to SEQ ID NO: 26.~~

~~232. The kit of claim 231, wherein the soluble IL-15 comprises a sequence that is 95% identical to SEQ ID NO: 26.~~

~~233. The kit of claim 232, wherein the soluble IL-15 comprises SEQ ID NO: 26.~~

~~234. The kit of any one of claims 228-233, wherein the sushi domain of IL15R α comprises a sushi domain from human IL15R α .~~

~~235. The kit of claim 234, wherein the sushi domain from human IL15R α comprises a sequence that is 80% identical to SEQ ID NO: 24.~~

~~236. The kit of claim 235, wherein the sushi domain from human IL15R α comprises a sequence that is 90% identical to SEQ ID NO: 24.~~

~~237. The kit of claim 236, wherein the sushi domain from human IL15R α comprises a sequence that is 95% identical to SEQ ID NO: 24.~~

~~238. The kit of claim 237, wherein the sushi domain from human IL15R α comprises SEQ ID NO: 24.~~

~~239. The kit of claim 234, wherein the sushi domain from human IL15R α is a mature full-length IL15R α .~~

~~240. The kit of any one of claims 200-227, wherein the pair of affinity domains in the first multi-chain chimeric polypeptide is selected from the group consisting of: barnase and barnstar, a PKA and an AKAP, adapter/docking tag modules based on mutated RNase I fragments, and SNARE modules based on interactions of the proteins syntaxin, synaptotagmin, synaptobrevin, and SNAP25.~~

~~241. The kit of any one of claims 200-240, wherein the first target-binding domain and the second target-binding domain in the first multi-chain chimeric polypeptide are each independently a soluble IL-15 or a soluble IL-18.~~

~~242. The kit of any one of claims 200-241, wherein the first target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-12, and the second target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-18.~~

~~243. The kit of any one of claims 200-241, wherein the first target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-18, and the second target-binding domain in the first multi-chain chimeric polypeptide binds specifically to a receptor for IL-12.~~

~~244. The kit of claim 252, wherein the first target-binding domain in the first multi-chain chimeric polypeptide comprises a soluble IL-18.~~

~~245. The kit of claim 244, wherein the soluble IL-18 is a soluble human IL-18.~~

~~246. The kit of claim 245, wherein the soluble human IL-18 comprises a sequence at least 80% identical to SEQ ID NO: 20.~~

~~247. The kit of claim 246, wherein the soluble human IL-18 comprises a sequence at least 90% identical to SEQ ID NO: 20.~~

~~248. The kit of claim 247, wherein the soluble human IL-18 comprises a sequence at least 95% identical to SEQ ID NO: 20.~~

~~249. The kit of claim 248, wherein the soluble human IL-18 comprises a sequence of SEQ ID NO: 20.~~

~~250. The kit of any one of claims 243-249, wherein the second target-binding domain in the first multi-chain chimeric polypeptide comprises a soluble IL-12.~~

~~251. The kit of claim 250, wherein the soluble IL-12 is a soluble human IL-12.~~

~~252. The kit of claim 251, wherein the soluble human IL-12 comprises a sequence of soluble human IL-12 β (p40) and a sequence of soluble human IL-12 α (p35).~~

~~253. The kit of claim 252, wherein the soluble human IL-15 further comprises a linker sequence between the sequence of soluble IL-12 β (p40) and the sequence of soluble human IL-12 α (p35).~~

~~254. The kit of claim 253, wherein the linker sequence comprises SEQ ID NO: 11.~~

~~255. The kit of any one of claims 252-254, wherein the sequence of soluble human IL-12 β (p40) comprises a sequence that is at least 80% identical to SEQ ID NO: 14.~~

~~256. The kit of claim 255, wherein the sequence of soluble human IL-12 β (p40) comprises a sequence that is at least 90% identical to SEQ ID NO: 14.~~

~~257. The kit of claim 256, wherein the sequence of soluble human IL-12 β (p40) comprises a sequence that is at least 95% identical to SEQ ID NO: 14.~~

~~258. The kit of claim 257, wherein the sequence of soluble human IL-12 β (p40) comprises SEQ ID NO: 14.~~

~~259. The kit of any one of claims 252-258, wherein the sequence of soluble human IL-12 α (p35) comprises a sequence that is at least 80% identical to SEQ ID NO: 16.~~

~~260. The kit of claim 259, wherein the sequence of soluble human IL-12 α (p35) comprises a sequence that is at least 90% identical to SEQ ID NO: 16.~~

~~261. The kit claim 260, wherein the sequence of soluble human IL-12 α (p35) comprises a sequence that is at least 95% identical to SEQ ID NO: 16.~~

~~262. The kit of claim 261, wherein the sequence of soluble human IL-12 α (p35) comprises SEQ ID NO: 16.~~

~~263. The kit of claim 200, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 63.~~

~~264. The kit of claim 263, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 63.~~

~~265. The kit of claim 264, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 63.~~

~~266. The kit of claim 265, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises SEQ ID NO: 63.~~

~~267. The kit of claim 266, wherein the first chimeric polypeptide in the first multi-chain chimeric polypeptide comprises SEQ ID NO: 64.~~

~~268. The kit of any one of claims 200 and 263-267, wherein the second chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 65.~~

~~269. The kit of claim 268, wherein the second chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 65.~~

~~270. The kit of claim 269, wherein the second chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 65.~~

~~271. The kit of claim 270, wherein the second chimeric polypeptide comprises SEQ ID NO: 65.~~

~~272. The kit of claim 271, wherein the second chimeric polypeptide comprises SEQ ID NO: 66.~~

~~273. The kit of any one of claims 200-272, wherein the first target-binding domain and the linker domain in the first chimeric polypeptide in the second multi-chain chimeric polypeptide directly abut each other in the first chimeric polypeptide.~~

~~274. The kit of any one of claims 200-272, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a linker~~

~~sequence between the first target binding domain and the linker domain in the first chimeric polypeptide.~~

~~275. The kit of any one of claims 200-274, wherein the linker domain and the first domain of the pair of affinity domains directly abut each other in the first chimeric polypeptide in the second multi-chain chimeric polypeptide.~~

~~276. The kit of any one of claims 200-274, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a linker sequence between the linker domain and the first domain of the pair of affinity domains in the first chimeric polypeptide.~~

~~277. The kit of any one of claims 200-276, wherein the second domain of the pair of affinity domains and the second target binding domain in the second chimeric polypeptide of the second multi-chain chimeric polypeptide directly abut each other in the second chimeric polypeptide.~~

~~278. The kit of any one of claims 200-276, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a linker sequence between the second domain of the pair of affinity domains and the second target binding domain in the second chimeric polypeptide.~~

~~279. The kit of any one of claims 200-278, wherein the linker domain is a soluble tissue factor domain.~~

~~280. The kit of claim 279, wherein the soluble tissue factor domain is a soluble human tissue factor domain.~~

~~281. The kit of claim 280, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 5.~~

~~282. The kit of claim 281, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 5.~~

~~283. The kit of claim 282, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 5.~~

~~284. The kit of claim 283, wherein the soluble human tissue factor domain comprises SEQ ID NO: 5.~~

~~285. The kit of claim 280, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 9.~~

~~286. The kit of claim 285, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 9.~~

~~287. The kit of claim 284, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 9.~~

~~288. The kit of claim 285, wherein the soluble human tissue factor domain comprises SEQ ID NO: 9.~~

~~289. The kit of claim 278, wherein the soluble human tissue factor domain comprises a sequence that is at least 80% identical to SEQ ID NO: 10.~~

~~290. The kit of claim 289, wherein the soluble human tissue factor domain comprises a sequence that is at least 90% identical to SEQ ID NO: 10.~~

~~291. The kit of claim 290, wherein the soluble human tissue factor domain comprises a sequence that is at least 95% identical to SEQ ID NO: 3.~~

~~292. The kit of claim 291, wherein the soluble human tissue factor domain comprises SEQ ID NO: 10.~~

~~293. The kit of any one of claims 279-281, 283-285, and 289-291, wherein the soluble human tissue factor domain does not comprise one or more of:~~

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~
~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~
~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~
~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~
~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~
~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~
~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

294. The kit of claim 293, wherein the soluble human tissue factor domain does not comprise any of:

~~a lysine at an amino acid position that corresponds to amino acid position 20 of mature wildtype human tissue factor protein;~~
~~an isoleucine at an amino acid position that corresponds to amino acid position 22 of mature wildtype human tissue factor protein;~~
~~a tryptophan at an amino acid position that corresponds to amino acid position 45 of mature wildtype human tissue factor protein;~~
~~an aspartic acid at an amino acid position that corresponds to amino acid position 58 of mature wildtype human tissue factor protein;~~
~~a tyrosine at an amino acid position that corresponds to amino acid position 94 of mature wildtype human tissue factor protein;~~
~~an arginine at an amino acid position that corresponds to amino acid position 135 of mature wildtype human tissue factor protein; and~~
~~a phenylalanine at an amino acid position that corresponds to amino acid position 140 of mature wildtype human tissue factor protein.~~

~~295. The kit of any one of claims 278-294, wherein the soluble tissue factor domain is not capable of binding to Factor VIIa.~~

~~296. The kit of any one of claims 278-295, wherein the soluble tissue factor domain does not convert inactive Factor X into Factor Xa.~~

~~297. The kit of any one of claims 278-296, wherein the second multi-chain chimeric polypeptide does not stimulate coagulation in a mammal.~~

~~298. The kit of any one of claims 198-297, wherein the first chimeric polypeptide and/or the second chimeric polypeptide in the second multi-chain chimeric polypeptide further comprises a signal sequence at its N-terminal end.~~

~~299. The kit of claim 298, wherein the signal sequence comprises SEQ ID NO: 28.~~

~~300. The kit of claim 299, wherein the signal sequence is SEQ ID NO: 28.~~

~~301. The kit of any one of claims 198-298, wherein the pair of affinity domains in the second multi-chain chimeric polypeptide is a sushi domain from an alpha chain of human IL-15 receptor (IL15R α) and a soluble IL-15.~~

~~302. The kit of claim 301, wherein the soluble IL-15 has a D8N or D8A amino acid substitution.~~

~~303. The kit of claim 301, wherein the soluble IL-15 comprises a sequence that is 80% identical to SEQ ID NO: 26.~~

~~304. The kit of claim 303, wherein the soluble IL-15 comprises a sequence that is 90% identical to SEQ ID NO: 26.~~

~~305. The kit of claim 304, wherein the soluble IL-15 comprises a sequence that is 95% identical to SEQ ID NO: 26.~~

~~306. The kit of claim 305, wherein the soluble IL-15 comprises SEQ ID NO: 26.~~

~~307. The kit of any one of claims 301-306, wherein the sushi domain of IL15R α comprises a sushi domain from human IL15R α .~~

~~308. The kit of claim 307, wherein the sushi domain from human IL15R α comprises a sequence that is 80% identical to SEQ ID NO: 24.~~

~~309. The kit of claim 308, wherein the sushi domain from human IL15R α comprises a sequence that is 90% identical to SEQ ID NO: 24.~~

~~310. The kit of claim 309, wherein the sushi domain from human IL15R α comprises a sequence that is 95% identical to SEQ ID NO: 24.~~

~~311. The kit of claim 310, wherein the sushi domain from human IL15R α comprises SEQ ID NO: 24.~~

~~312. The kit of claim 307, wherein the sushi domain from human IL15R α is a mature full-length IL15R α .~~

~~313. The kit of any one of claims 200-300, wherein the pair of affinity domains in the second multi-chain chimeric polypeptide is selected from the group consisting of: barnase and barnstar, a PKA and an AKAP, adapter/docking tag modules based on mutated RNase I fragments, and SNARE modules based on interactions of the proteins syntaxin, synaptotagmin, synaptobrevin, and SNAP25.~~

~~314. The kit of any one of claims 200-313, wherein the first target-binding domain and the second target-binding domain in the second multi-chain chimeric polypeptide are each independently a soluble IL-7 or a soluble IL-21.~~

~~315. The kit of any one of claims 200-314, wherein the first target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a~~

receptor for IL-21, and the second target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-7.

~~316. The kit of any one of claims 200-314, wherein the first target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-7, and the second target-binding domain in the second multi-chain chimeric polypeptide binds specifically to a receptor for IL-21.~~

~~317. The kit of claim 316, wherein the first target-binding domain in the second multi-chain chimeric polypeptide comprises a soluble IL-21.~~

~~318. The kit of claim 317, wherein the soluble IL-21 is a soluble human IL-21.~~

~~319. The kit of claim 318, wherein the soluble human IL-21 comprises a sequence at least 80% identical to SEQ ID NO: 22.~~

~~320. The kit of claim 319, wherein the soluble human IL-21 comprises a sequence at least 90% identical to SEQ ID NO: 22.~~

~~321. The kit of claim 320, wherein the soluble human IL-21 comprises a sequence at least 95% identical to SEQ ID NO: 22.~~

~~322. The kit of claim 321, wherein the soluble human IL-21 comprises a sequence of SEQ ID NO: 22.~~

~~323. The kit of any one of claims 316-322, wherein the second target-binding domain comprises a soluble IL-7.~~

~~324. The kit of claim 323, wherein the soluble IL-7 is a soluble human IL-7.~~

~~325. The kit of claim 324, wherein the soluble human IL-7 comprises a sequence at least 80% identical to SEQ ID NO: 23.~~

~~326. The kit of claim 325, wherein the soluble human IL-7 comprises a sequence at least 90% identical to SEQ ID NO: 23.~~

~~327. The kit of claim 326, wherein the soluble human IL-7 comprises a sequence at least 95% identical to SEQ ID NO: 23.~~

~~328. The kit of claim 327, wherein the soluble human IL-7 comprises a sequence of SEQ ID NO: 23.~~

~~329. The kit of claim 200, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 67.~~

~~330. The kit of claim 329, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 67.~~

~~331. The kit of claim 330, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 67.~~

~~332. The kit of claim 331, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 67.~~

~~333. The kit of claim 332, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 68.~~

~~334. The kit of any one of claims 200 and 329-333, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 69.~~

~~335. The kit of claim 334, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 69.~~

~~336. The kit of claim 335, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 69.~~

~~337. The kit of claim 336, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 69.~~

~~338. The kit of claim 337, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 70.~~

~~339. The kit of claim 200, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 71.~~

~~340. The kit of claim 339, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 71.~~

~~341. The kit of claim 340, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 71.~~

~~342. The kit of claim 341, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 71.~~

~~343. The kit of claim 342, wherein the first chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 72.~~

~~——— 344. The kit of any one of claims 200 and 339-343, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 80% identical to SEQ ID NO: 73.~~

~~345. The kit of claim 344, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 90% identical to SEQ ID NO: 73.~~

~~346. The kit of claim 345, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises a sequence that is at least 95% identical to SEQ ID NO: 73.~~

~~347. The kit of claim 346, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 73.~~

~~348. The kit of claim 347, wherein the second chimeric polypeptide in the second multi-chain chimeric polypeptide comprises SEQ ID NO: 74.~~

~~349. The kit of any one of claims 200-348, wherein the IgG1 antibody construct is a monoclonal IgG1 antibody, where both antigen-binding domains in the monoclonal IgG1 antibody bind specifically to the linker domain.~~

~~350. The kit of any one of claims 200-348, wherein the IgG1 antibody construct is a bispecific IgG1 antibody, where one of the two antigen-binding domains in the bispecific IgG1 antibody binds specifically to the linker domain.~~