

What is claimed:

1. A method for preventing atherosclerosis in a subject, comprising administering to the subject in need thereof, a therapeutically effective amount of a peptide that affects the interaction of CD40 with CD154/CD40-ligand.
- 5 2. The method of claim 1, wherein the peptide binds to CD40.
3. The method of any of the prior claims, wherein said peptide binds to a CD40 protein with a K_d of greater than 10^{-6} .
4. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 and CD154.
- 10 5. The method of any of the prior claims, wherein said peptide inhibits the binding of CD40 to CD154.
6. The method of any of the prior claims, wherein said peptide binds CD40 at the site where CD40 interacts with CD154.
7. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to prevent the expansion of Th40 cells.
- 15 8. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to reduce the number of Th40 cells.
9. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as alter the cytokine expression profile of a cell population treated with said peptide.
- 20 10. The method of any of the prior claims, wherein said peptide comprises an amino acid sequence selected from the group of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, and SEQ ID NO:30.
- 25 11. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, and SEQ ID NO:30.
12. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:3-9, 24-30, and 32.
- 30

13. The method of any of the prior claims, wherein the subject does not produce autoantibodies responsive to the peptide and/or CD154.
14. The method of any of the prior claims, wherein the subject's T cells do not elicit T cell antigen recall.
- 5 15. The method of any of the prior claims, wherein said peptide binds to multiple bone marrow derived cell types which express CD40 of approximately 45kDa, including splenic CD4hi cells, CD8 cells, and other antigen presenting cells.
16. The method of any of the prior claims, wherein said peptide is obtained from natural sources or it is synthesized.
- 10 17. The method of any of the prior claims, wherein the subject suffers from dyslipidemia, hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disease, and/or coronary heart disease.
18. The method of any of the prior claims, further comprising administering a statin.
19. A method to modulate atherosclerosis comprising contacting a CD40 protein with a
15 peptide that binds said CD40 protein at the CD154-binding site in such a manner as to modulate atherosclerosis.
20. A method of modulating atherosclerosis in a patient comprising administering to a patient a peptide that binds to a CD40 protein at the CD154-binding site and thereby modulates atherosclerosis.
- 20 21. A method of treating cardiovascular disease in a patient in need of such treatment comprising administering to a patient a peptide that binds to a CD40 protein at the CD154-binding site and thereby modulates cardiovascular disease.
22. The method of any of the prior claims, further comprising reducing the number of Th40 cells in a patient by administering a compound that inhibits the interaction of CD40
25 and CD154, wherein said compound binds the CD40 protein at the CD154-binding site.
23. A method of reversing atherosclerosis in an animal comprising administering to a patient a peptide that binds to CD40 protein at the CD154-binding site and thereby modulates inflammation.
24. A method to identify a patient at risk for developing atherosclerosis, said method
30 comprising (a) obtaining a population of T-cells from a patient; and (b) determining the number of cells that are CD40+ in the T-cell population, wherein if the percentage of

CD40+ T-cells in the T-cell population is greater than 25%, said patient is at risk for developing atherosclerosis.

25. A method for preventing progression of atherosclerosis comprising reducing the number of Th40 cells in a patient.

5 26. The method of any of the prior claims, further comprising administering a compound that inhibits the interaction of CD40 and CD154, wherein the said compound binds the CD protein at the CD154-binding site.

27. A method to modulate and/or reduce atherosclerosis in an animal, the method comprising administering to the animal, a peptide that interacts with a CD40 protein in such a manner as to
10 modulate INF γ .

28. A method to identify a patient at risk for developing cardiovascular disease and/or atherosclerosis, the method comprising obtaining a sample containing T-cells from a patient to be tested, contacting the sample with a peptide that binds the CD40 protein, detecting the CD-40 bound peptide, and determining the level of Th40 cells from the amount of CD40 bound,
15 wherein a level of Th40 cells greater than 25% of the total T-cell population indicates the patient is at risk for developing cardiovascular disease and/or developing atherosclerosis.

29. A method to prevent, modulate, or reduce calcification of vessel walls, the method comprising administering to the subject in need thereof, a therapeutically effective amount of a peptide which specifically binds to a CD40 presenting cells at the CD154 binding site.

20 30. The method of any of the prior claims, wherein the peptide binds to CD40.

31. The method of any of the prior claims, wherein said peptide binds to a CD40 protein with a Kd of greater than 10^{-6} .

32. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 and CD154.

25 33. The method of any of the prior claims, wherein said peptide inhibits the binding of CD40 to CD154.

34. The method of any of the prior claims, wherein said peptide binds CD40 at the site where CD40 interacts with CD154.

35. The method of any of the prior claims, wherein said peptide affects the interaction of
30 CD40 with CD154 in such a manner as to prevent the expansion of Th40 cells.

36. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to reduce the number of Th40 cells.
37. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as alter the cytokine expression profile of a cell population
5 treated with said peptide.
38. The method of any of the prior claims, wherein said peptide comprises an amino acid sequence selected from the group of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.
39. The method of any of the prior claims, wherein said peptide comprises an amino acid
10 sequence selected from the group of SEQ ID NO:3-9 and 24-30.
40. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO:29, SEQ ID NO: 30, and SEQ ID NO:32.
- 15 41. A method to administer a CD40-binding peptide to prevent, modulate, and/or reduce atherosclerosis, comprising selecting a peptide that interacts with a CD40 protein and CD154 binding site, selecting a delivery method selected from the group comprising intramuscular (IM) delivery, intravenous (IV) delivery, subcutaneous (SC) delivery, oral delivery, gavage delivery, emollient/skin delivery, or transdermal patch.
- 20 42. A method to administer a peptide that affects the CD40-CD154 to prevent, modulate, and/or reduce atherosclerosis in an animal, comprising selecting a peptide that interacts with a CD40 protein and CD154 binding site and using an extended delivery method selected from the group comprising an implantable device, a hydrophilic polymer formulation, a permeable polymeric membrane, injectable gel implants, solvent extraction system, phase inversion system,
25 thermosensitive gels, pH dependent *in situ* gels, microparticles, microspheres, nanoparticles, nanospheres, bio-degradable implants, or photoactivated depot.
43. A method to lower LDL cholesterol in a subject, the method comprising administering to the subject in need thereof, a therapeutically effective amount of a peptide which specifically binds to a CD40 presenting cells at the CD154 binding site.
- 30 44. The method of any of the prior claims, wherein the peptide binds to CD40.

45. The method of any of the prior claims, wherein said peptide binds to a CD40 protein with a Kd of greater than 10^{-6} .
46. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 and CD154.
- 5 47. The method of any of the prior claims, wherein said peptide inhibits the binding of CD40 to CD154.
48. The method of any of the prior claims, wherein said peptide binds CD40 at the site where CD40 interacts with CD154.
49. The method of any of the prior claims, wherein said peptide affects the interaction of
10 CD40 with CD154 in such a manner as alter the cytokine expression profile of a cell population treated with said peptide.
50. The method of any of the prior claims, wherein said peptide comprises an amino acid sequence selected from the group of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.
- 15 51. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO:29, and SEQ ID NO: 30.
52. A method for preventing, modulating, reducing, treating, and/or reversing type 2 diabetes
20 in a subject, comprising administering to the subject having type 2 diabetes, a therapeutically effective amount of a peptide that affects the interaction of CD40 with CD154/CD40-ligand.
53. The method of any of the prior claims, wherein the peptide binds to CD40.
54. The method of any of the prior claims, wherein said peptide binds to a CD40 protein with a Kd of greater than 10^{-6} .
- 25 55. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 and CD154.
56. The method of any of the prior claims, wherein said peptide inhibits the binding of CD40 to CD154.
57. The method of any of the prior claims, wherein said peptide binds CD40 at the site where
30 CD40 interacts with CD154.

58. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to prevent the expansion of Th40 cells.
59. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to reduce the number of Th40 cells.
- 5 60. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to alter the cytokine expression profile of a cell population treated with said peptide.
61. The method of any of the prior claims, wherein said peptide comprises an amino acid sequence selected from the group of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID
10 NO:6, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:27.
62. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:27.
63. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:4-9 and 24-30.
- 15 64. A method for modulating and/or increasing glucose transport protein 4 (GLUT4), the method comprising administering to a patient a therapeutically sufficient dose of a peptide selected from SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:27.
65. A method for modulating and/or increasing glucose transport protein 4 (GLUT4), the
20 method comprising administering to a patient a therapeutically sufficient dose of a peptide selected from the group of SEQ ID NO:4-9 and 24-30.
66. A method for preventing, modulating, reducing, treating, and/or reversing type 2 diabetes in a subject, the method comprising administering to the animal, a peptide that interacts with the CD40 protein in such a manner as to modulate GLUT 4.
- 25 67. The method of any of the prior claims, wherein the subject does not produce autoantibodies responsive to the peptide and/or CD154 and/or GLUT 4.
68. The method of any of the prior claims, wherein the subject's T cells do not elicit T cell antigen recall.
69. The method of any of the prior claims, wherein said peptide binds to multiple bone
30 marrow derived cell types which express CD40 of approximately 45kDa, including splenic CD4hi cells, CD8 cells, and other antigen presenting cells.

70. The method of any of the prior claims, wherein said peptide is obtained from natural sources or it is synthesized.

71. A method of modulating type 2 diabetes in a patient comprising administering to a patient a peptide that binds to a CD40 protein at the CD154-binding site and thereby modulates type 2 diabetes.

72. A method to administer a CD40-binding peptide to prevent, modulate, reduce, treat, and/or reverse type 2 diabetes in a subject, comprising selecting a peptide that interacts with a CD40 protein and CD154 binding site, selecting a delivery method from the group comprising intramuscular (IM) delivery, intravenous (IV) delivery, subcutaneous (SC) delivery, oral delivery, gavage delivery, emolument/skin delivery, or transdermal patch.

73. A method to administer a CD40-binding peptide to prevent, modulate, reduce, treat and/or reverse type 2 diabetes in a subject, comprising selecting a peptide that interacts with a CD40 protein and CD154 binding site, using an extended delivery method selected from the group comprising an implantable device, a hydrophilic polymer formulation, a permeable polymeric membrane, injectable gel implants, solvent extraction system, phase inversion system, thermosensitive gels, pH dependent *in situ* gels, microparticles, microspheres, nanoparticles, nanospheres, bio-degradable implants, or photoactivated depot.

74. A method to modulate and/or reduce type 2 diabetes in a subject, the method comprising administering to the subject, a peptide that interacts with a CD40 protein in such a manner as to modulate $\text{INF}\gamma$.

75. A method to modulate and/or reduce $\text{INF-}\gamma$ in a cell or a subject comprising administering a peptide selected from SEQ ID NOs 3-9 and 27-30, in an amount sufficient to reduce or inhibit $\text{INF-}\gamma$ signaling, wherein, the $\text{INF-}\gamma$ signaling is associated with type 2 diabetes.

76. A method to modulate and/or reduce interleukin-2 signaling in a cell or a subject comprising administering a peptide selected from SEQ ID NOs 3-9 and 27-30, in an amount sufficient to reduce or inhibit interleukin-2 signaling, wherein, the interleukin-2 signaling is associated with type 2 diabetes.

77. A method to modulate and/or reduce interleukin 17 (IL-17) in a cell or a subject comprising administering a peptide selected from SEQ ID NOs 3-9 and 27-30, in an amount sufficient to reduce or inhibit interleukin 17 (IL-17) signaling, wherein, the IL-17 is associated with type 2 diabetes.

78. A method to modulate and/or reduce interleukin 17 (IL-17) in a cell or a subject comprising administering a peptide selected from SEQ ID NOs 3-9 and 27-30, in an amount sufficient to reduce or inhibit interleukin 17 (IL-17) signaling, wherein, the IL-17 signaling is associated with a condition selected from the group comprising type I diabetes, type 2 diabetes, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, inflammatory bowel disease, chronic obstructive pulmonary disease, asthma, atherosclerosis, vasculitis, hypertension, thyroiditis, primary biliary cirrhosis, Paget's disease, Addison's disease, acute respiratory distress syndrome, acute lung injury, and/or aseptic chronic inflammation, more generally.
79. A method to identify a patient at risk for developing type 2 diabetes, the method comprising obtaining a sample containing T-cells from a patient to be tested, contacting the sample with a peptide that binds the CD40 protein, detecting the CD-40 bound peptide, and determining the level of Th40 cells from the amount of CD40 bound, wherein a level of Th40 cells greater than 25% of the total T-cell population indicates the patient is at risk for developing type 2 diabetes.
80. A method to identify a patient at risk for developing autoimmune disease and/or type 2 diabetes, the method comprising obtaining a sample containing T-cells from a patient to be tested, contacting the sample with a peptide that binds the CD40 protein, detecting the CD-40 bound peptide, and determining the level of Th40 cells from the amount of CD40 bound, wherein a level of Th40 cells greater than 25% of the total T-cell population indicates the patient is at risk for developing autoimmune disease and/or developing type 2 diabetes.
81. A method to prevent, modulate, or reduce autoimmune disease and/or type 2 diabetes, the method comprising administering to the subject in need thereof, a therapeutically effective amount of a peptide which specifically binds to a CD40 presenting cells at the CD154 binding site.
82. The method of any of the prior claims, wherein the peptide binds to CD40.
83. The method of any of the prior claims, wherein said peptide binds to a CD40 protein with a Kd of greater than 10^{-6} .
84. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 and CD154.

85. The method of any of the prior claims, wherein said peptide inhibits the binding of CD40 to CD154.
86. The method of any of the prior claims, wherein said peptide binds CD40 at the site where CD40 interacts with CD154.
- 5 87. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to prevent the expansion of Th40 cells.
88. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to reduce the number of Th40 cells.
89. The method of any of the prior claims, wherein said peptide affects the interaction of
10 CD40 with CD154 in such a manner as alter the cytokine expression profile of a cell population treated with said peptide.
90. The method of any of the prior claims, wherein said peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:27, SEQ ID NO:28,
15 SEQ ID NO:29, and SEQ ID NO:30.
91. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, and SEQ ID NO:30.
92. The method of any of the prior claims, wherein said peptide is an amino acid sequences
20 selected from the group of SEQ ID NOs:3-9, 24-30 and 32.
93. A method for preventing, modulating, reducing, treating, and/or reversing autoimmune and/or auto-inflammatory disease in a subject, comprising administering to the subject having type 2 diabetes, a therapeutically effective amount of a peptide that affects the interaction of CD40 with CD154/CD40-ligand.
- 25 94. A method for preventing, modulating, reducing, treating, and/or reversing autoimmune and auto-inflammatory disease in a subject, comprising administering a therapeutically effective amount of a peptide that affects the interaction of CD40 with CD154/CD40-ligand, wherein the subject suffers from a condition selected from the group comprising type I diabetes, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, inflammatory
30 bowel disease, chronic obstructive pulmonary disease, asthma, atherosclerosis, vasculitis, hypertension, thyroiditis, primary biliary cirrhosis, Paget's disease, Addison's disease, acute

respiratory distress syndrome, acute lung injury, type 2 diabetes, and/or aseptic chronic inflammation, more generally.

95. A method for preventing, modulating, reducing, treating, and/or reversing autoimmune and/or autoinflammatory disease in a subject, comprising administering to the subject having
5 autoimmune and/or autoinflammatory disease, a peptide that interacts with the CD40 protein in such a manner as to modulate GLUT 4.

96. A method for preventing, modulating, reducing, treating, and/or reversing autoimmune and/or autoinflammatory disease in a subject, comprising administering to the subject having autoimmune and/or autoinflammatory disease, a peptide that interacts with a CD40 protein in
10 such a manner as to modulate INF γ .

98. A method for preventing, modulating, reducing, treating, and/or reversing autoimmune and/or autoinflammatory disease in a subject, comprising administering to the subject having autoimmune and/or autoinflammatory disease, a peptide that interacts with a CD40 protein in such a manner as to modulate interleukin-2 (IL-2).

99. A method for preventing, modulating, reducing, treating, and/or reversing autoimmune and/or autoinflammatory disease in a subject, comprising administering to the subject having autoimmune and/or autoinflammatory disease, a peptide that interacts with a CD40 protein in
15 such a manner as to modulate interleukin-17 (IL-17).

100. A method of any of the prior claims, wherein the peptide binds to CD40.

101. The method of any of the prior claims, wherein said peptide binds to a CD40 protein with
20 a K_d of greater than 10⁻⁶.

102. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 and CD154.

103. The method of any of the prior claims, wherein said peptide inhibits the binding of CD40
25 to CD154.

104. The method of any of the prior claims, wherein said peptide binds CD40 at the site where CD40 interacts with CD154.

105. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to prevent the expansion of Th40 cells.

106. The method of any of the prior claims, wherein said peptide affects the interaction of
30 CD40 with CD154 in such a manner as to reduce the number of Th40 cells.

107. The method of any of the prior claims, wherein said peptide affects the interaction of CD40 with CD154 in such a manner as to alter the cytokine expression profile of a cell population treated with said peptide.
108. The method of any of the prior claims, wherein said peptide comprises an amino acid
5 sequence selected from the group of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO: 29, and SEQ ID NO:30.
109. The method of any of the prior claims, wherein said peptide is an amino acid sequence selected from the group of SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID
10 NO:27, SEQ ID NO:28, SEQ ID NO: 29, and SEQ ID NO:30.
110. The method of any of the prior claims, wherein said peptide binds to multiple bone marrow derived cell types which express CD40 of approximately 45kDa, including splenic CD4hi cells, CD8 cells, and other antigen presenting cells.
111. The method of any of the prior claims, wherein said peptide is obtained from natural
15 sources or it is synthesized.
112. The method of any of the prior claims, wherein the CD40-binding peptide is administered to the subject via a delivery method selected from the group comprising intramuscular (IM) delivery, intravenous (IV) delivery, subcutaneous (SC) delivery, oral delivery, gavage delivery, emolument/skin delivery, transdermal patch, or nasal administration.
113. The method of any of the prior claims, wherein the CD40-binding peptide is administered
20 to the subject via a delivery method selected from the group comprising an implantable device, a hydrophilic polymer formulation, a permeable polymeric membrane, injectable gel implants, solvent extraction system, phase inversion system, thermosensitive gels, pH dependent *in situ* gels, microparticles, microspheres, nanoparticles, nanospheres, bio-degradable implants, or
25 photoactivated depot.
114. A composition, method or system as described herein.