CLAIMS

The invention claimed is:

1. An *in vitro* method for ~~modulating~~ inhibiting cell fusion of a hematopoietic cell expressing an intermediate-conductance calcium-activated potassium (SK4) channel, the method comprising the step of contacting the cell with an effective amount of an SK4 channel inhibitor ~~or activator~~, wherein said cell fusion is ~~modulated~~inhibited.

~~2. The method of claim 1, wherein cell fusion is inhibited.~~

~~3. The method of claim 1, wherein the cell is a hematopoietic cell.~~

42. The method of claim 1, wherein the hematopoietic cell is selected from the group consisting of a macrophage, dendritic cell, and B-cell.

53. The method of claim 1, wherein the hematopoietic cell is a macrophage, and wherein the cell fusion is homotypic or heterotypic.

64. The method of claim 1, wherein the cell fusion is homotypic or heterotypic.

75. The method of ~~claim 1~~any one of claims 1-4, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.

86. The method of claim 75, wherein said inhibitory nucleic acid targets expression of an SK4 channel comprising the sequence set forth in SEQ ID NO:2.

97. The method of claim 75, wherein the monoclonal antibody recognizes a pore region or small molecule-binding domain of an SK4 channel.

108. The method of claim 75, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]

-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl) diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.

~~11~~9. The method of claim ~~7~~5, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.

~~12~~10. The method of claim ~~7~~5, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.

~~13~~11. The method of claim ~~7~~5, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.

~~14~~12. The method of claim ~~7~~5, further comprising the step of assaying for SK4 channel expression or activity in the cell.

13. Use of an SK4 channel inhibitor in the manufacture of a medicament for use in an *in vivo* method for inhibiting cell fusion of a hematopoietic cell expressing an intermediate-conductance calcium-activated potassium (SK4) channel, the method comprising the step of contacting the cell with an effective amount of said SK4 channel inhibitor, wherein said cell fusion is inhibited.

14. The use of claim 13, wherein the hematopoietic cell is selected from the group consisting of a macrophage, dendritic cell, and B-cell.

15. The use of claim 13, wherein the hematopoietic cell is a macrophage and wherein the cell fusion is homotypic or heterotypic.

16. The use of claim 13, wherein the cell fusion is homotypic or heterotypic.

17. The use of any one of claims 13-16, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.

18. The use of claim 17, wherein said inhibitory nucleic acid targets expression of an SK4 channel comprising the sequence set forth in SEQ ID NO:2.

19. The use of claim 17, wherein the monoclonal antibody recognizes a pore region or small molecule-binding domain of an SK4 channel.

20. The use of claim 17, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl) diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl) diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.

21. The use of claim 17, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.

22. The use of claim 17, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.

23. The use of claim 17, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.

24. The use of claim 17, further comprising the step of assaying for SK4 channel expression or activity in the cell.

25. The use of any one of claims 13-24, wherein the effective amount of the SK4 channel inhibitor is a therapeutically effective amount provided to a subject having or suspected of having abnormal hematopoietic cell fusion.

26. The use of claim 25, further comprising co-providing to the subject a therapeutically effective amount of an anti-inflammatory agent, anti-bone-loss agent, immunosuppressive agent, or chemotherapeutic agent.

27. The use of claim 25 or 26, wherein said hematopoietic cell is a macrophage cell, and wherein said medicament is for use in preventing or treating a disease or disorder that is mediated by macrophage-derived multinucleate cells.

28. The use of claim 27, wherein said disease or disorder is a bone disease associated with bone loss, an autoimmune or inflammatory disease, rejection of an implant or transplant, or cancer metastasis.

~~15. An *in vitro* method for modulating osteoclast differentiation and function, the method comprising the step of contacting an osteoclast or an osteoclast precursor with an effective amount of an intermediate-conductance potassium-activated potassium (SK4) channel inhibitor or activator.~~

~~16. The method of claim 15, wherein osteoclast formation is inhibited.~~

~~17. The method of claim 15, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.~~

~~18. The method of claim 17, wherein the monoclonal antibody recognizes a pore region or small molecule-binding domain of an SK4 channel.~~

~~19. The method of claim 17, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.~~

~~20. The method of claim 17, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.~~

~~21. The method of claim 17, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.~~

~~22. The method of claim 17, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.~~

~~23. Use of an intermediate-conductance calcium-activated potassium (SK4) channel inhibitor in the manufacture of a medicament for preventing or treating bone loss in a subject susceptible to or having bone loss, wherein said intermediate-conductance calcium-activated potassium (SK4) channel inhibitor is present in said medicament in a therapeutically effective amount to inhibit osteoclast formation.~~

~~24. The use of claim 23, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.~~

~~25. The use of claim 24, wherein the monoclonal antibody recognizes a pore region, or a small molecule-binding domain of an SK4 channel.~~

~~26. The use of claim 24, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.~~

~~27. The use of claim 24, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.~~

~~28. The use of claim 24, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.~~

~~29. The use of claim 24, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.~~

~~30. The use of claim 23, further comprising a therapeutically effective amount of an anti-inflammatory agent, anti-bone-loss agent, immunosuppressive agent or chemotherapeutic agent to be co-administered with said medicament.~~

~~31. Use of an intermediate-conductance calcium-activated potassium (SK4) channel inhibitor in the manufacture of a medicament for preventing or treating an inflammatory or autoimmune disease characterized by giant cell formation in a subject susceptible to or having the inflammatory or autoimmune disease, wherein said intermediate-conductance calcium-activated potassium (SK4) channel inhibitor is present in said medicament in a therapeutically effective amount to inhibit giant cell formation.~~

~~32. The use of claim 31, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.~~

~~33. The use of claim 32, wherein the monoclonal antibody recognizes a pore region or small molecule-binding domain of an SK4 channel.~~

~~34. The use of claim 32, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.~~

~~35. The use of claim 32, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.~~

~~36. The use of claim 32, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.~~

~~37. The use of claim 32, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.~~

~~38. The use of claim 31, further comprising a therapeutically effective amount of an anti-inflammatory agent, anti-bone-loss agent, immunosuppressive agent, or chemotherapeutic agent to be co-administered with said medicament.~~

~~39. Use of an intermediate-conductance calcium-activated potassium (SK4) channel inhibitor for the manufacture of a medicament for preventing implant or transplant rejection in a subject having an implant or a transplant at a site located within the subject, wherein said intermediate-conductance calcium-activated potassium (SK4) channel inhibitor is present in said medicament in a therapeutically effective amount to inhibit giant cell formation at or in the vicinity of the site.~~

~~40. The use of claim 39, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.~~

~~41. The use of claim 40, wherein the monoclonal antibody recognizes a pore region or small molecule binding domain of an SK4 channel.~~

~~42. The use of claim 40, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl) diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.~~

~~43. The use of claim 40, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.~~

~~44. The use of claim 40, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.~~

~~45. The use of claim 40, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.~~

~~46. The use of claim 39, further comprising a therapeutically effective amount of an anti-inflammatory agent, or an immunosuppressive agent to be co-administered with said medicament.~~

~~47. The use of claim 39, wherein the transplant is a cell, organ, or tissue transplant.~~

~~48. Use of an intermediate-conductance calcium-activated potassium (SK4) channel inhibitor for the manufacture of a medicament to prevent cancer metastasis in a subject having cancer, wherein said intermediate-conductance calcium-activated potassium (SK4) channel inhibitor is present in said medicament in a therapeutically effective amount to inhibit metastatic cancer cell formation.~~

49. The use of claim 48, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.

50. The use of claim 49, wherein the monoclonal antibody recognizes a pore region or small molecule binding domain of an SK4 channel.

51. The use of claim 49, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl) diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.

52. The use of claim 49, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.

53. The use of claim 49, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.

54. The use of claim 49, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.

55. The use of claim 48, further comprising a therapeutically effective amount of an anti-inflammatory agent, anti-bone-loss agent, immunosuppressive agent or chemotherapeutic agent to be co-administered with said medicament.

56. A method to identify an intermediate-conductance calcium-activated potassium (SK4) channel inhibitor that inhibits cell-cell fusion, the method comprising the steps of:

contacting a cell population with a candidate SK4 channel inhibitor; and

determining whether the candidate agent inhibits cell-cell fusion within the cell population.

57. The method of claim 56, wherein the cell population comprises macrophages and the SK4 channel inhibitor inhibits cell-cell fusion of macrophages.

58. The method of claim 56, wherein the cell population comprises at least two cell types, one of which is macrophages.

59. A composition comprising:

an effective amount of an intermediate-conductance calcium-activated potassium (SK4) channel inhibitor; and

a therapeutic, wherein the therapeutic agent is selected from the group consisting of an anti-inflammatory agent, anti-bone-loss agent, immunosuppressive agent and chemotherapeutic agent.

60. The composition of claim 59, wherein the SK4 channel inhibitor is selected from the group consisting of an inhibitory nucleic acid, monoclonal antibody, and small molecule inhibitor.

61. The composition of claim 60, wherein the monoclonal antibody recognizes a pore region or small molecule binding domain of an SK4 channel.

62. The composition of claim 60, wherein the small molecule inhibitor is selected from the group consisting of 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole; 2,2-bis(4-fluorophenyl)-2-phenylacetamide; 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(4-chlorophenyl)diphenylmethyl]-1H-pyrazole; 1-[(2-fluorophenyl) diphenylmethyl]-1H-pyrazole; and 1-[(2-chlorophenyl)diphenylmethyl]-1H-tetrazole.

63. The composition of claim 60, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)-diphenylmethyl]-1H-imidazole.

64. The composition of claim 60, wherein the small molecule inhibitor is 2,2-bis(4-fluorophenyl)-2-phenylacetamide.

65. The composition of claim 60, wherein the small molecule inhibitor is 1-[(2-chlorophenyl)diphenylmethyl]-1H-pyrazole.

66. The composition of claim 59, further comprising a pharmaceutically acceptable carrier.