CLAIMS

1. An Fc construct comprising:

a) a first polypeptide having the formula A-L-B; wherein

i) A comprises a first Fc domain monomer;

ii) L is a glycine spacer; and

iii) B comprises a second Fc domain monomer;

b) a second polypeptide having the formula A'-L'-B'; wherein

i) A' comprises a third Fc domain monomer;

ii) L' is a glycine spacer; and

iii) B' comprises a fourth Fc domain monomer;

c) a third polypeptide that comprises a fifth Fc domain monomer; and

d) a fourth polypeptide that comprises a sixth Fc domain monomer;

wherein

each of the first and second polypeptides has at least 95% sequence identity to the sequence of DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRDKLT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGGGGDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLKSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 49),

each of the third and fourth polypeptides has at least 95% sequence identity to the sequence of DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPSRDELT KNQVSLSCAVDGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPG (SEQ ID NO: 48),

B and B' combine to form a first Fc domain, A and the fifth Fc domain monomer combine to form a second Fc domain, and A' and the sixth Fc domain monomer combine to form a third Fc domain,

each of B and B' comprises the mutations D399K and K409D, each of A and A' comprises the mutations S354C, T366W, and E357K, and each of the fifth and sixth Fc domain monomers comprises the mutations Y349C, T366S, L368A, Y407V, and K370D,

each of L and L' comprises 12-30 glycines, and

each of the first, second, third, and fourth polypeptides lack a C-terminal lysine.

2. The Fc construct of claim 1, wherein each of L and L' comprises the sequence of GGGGGGGGGGGGGGGGGGGG (SEQ ID NO: 27).

3. The Fc construct of claim 1, wherein the first polypeptide and the second polypeptide have the same amino acid sequence and wherein the third polypeptide and the fourth polypeptide have the same amino acid sequence.

4. The Fc construct of claim 1, wherein each of the first and second polypeptides comprises the sequence of
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT
KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRDKLT
KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGGGGDKTHTCPPCPAPELLGGPSVFLFPPK
PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLKSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID
NO: 49).

5. The Fc construct of claim 1, wherein each of the third and fourth polypeptides comprises the sequence of
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT
KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPSRDELT
KNQVSLSCAVDGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPG (SEQ ID NO: 48).

6. The Fc construct of claim 1, wherein each of the first and second polypeptides comprises the sequence of
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT
KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRDKLT
KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGGGGDKTHTCPPCPAPELLGGPSVFLFPPK
PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLKSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID
NO: 49), and
each of the third and fourth polypeptides comprises the sequence of

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT
KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPSRDELT
KNQVSLSCAVDGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPG (SEQ ID NO: 48).

7. An Fc construct comprising:

a). a first polypeptide having the formula A-L-B; wherein

i). A comprises a first Fc domain monomer;

ii). L is a linker; and

iii). B comprises a second Fc domain monomer;

b). a second polypeptide having the formula A'-L'-B'; wherein

i). A' comprises a third Fc domain monomer;

ii). L' is a linker; and

iii). B' comprises a fourth Fc domain monomer;

c). a third polypeptide comprises a fifth Fc domain monomer; and

d). a fourth polypeptide comprises a sixth Fc domain monomer;

wherein A of first polypeptide and A' of second polypeptide combine to form a first Fc domain, B of first polypeptide and fifth Fc domain monomer combine to form a second Fc domain, and B' of second polypeptide and sixth Fc domain monomer combine to form a third Fc domain; and
wherein the first and second polypeptide comprise the sequence of SEQ ID NO: 49, and the third and fourth polypeptide comprise the sequence of SEQ ID NO: 48.

8. The Fc construct of any one of claims 1-7, wherein the Fc construct has anti-inflammatory activity.

9. The Fc construct of any one of claims 1-8, wherein one or more of the Fc domain monomers is an IgG Fc domain monomer.

10. The Fc construct of any one of claims 1-9, wherein one or more of the Fc domain monomers is an IgG Fc domain monomer having up to ten amino acid modifications.

11. The Fc construct of any one of claims 1-9, wherein each Fc domain monomer has no more than ten amino acid modifications.

12. A pharmaceutical composition comprising the Fc construct of any one of claims 1-11.

13. Use of the Fc construct of any one of claims 1-11 in the manufacture of a medicament for the treatment of an autoimmune disease.

14. Use of the Fc construct of any one of claims 1-11 in the manufacture of a medicament for the treatment of inflammation.

15. A cell culture medium comprising a substantially homogenous population of an Fc construct comprising:

a) a first polypeptide having the formula A-L-B; wherein

i) A comprises a first Fc domain monomer;

ii) L is a glycine spacer; and

iii) B comprises a second Fc domain monomer;

b) a second polypeptide having the formula A'-L'-B'; wherein

i) A' comprises a third Fc domain monomer;

ii) L' is a glycine spacer; and

iii) B' comprises a fourth Fc domain monomer;

c) a third polypeptide that comprises a fifth Fc domain monomer; and

d) a fourth polypeptide that comprises a sixth Fc domain monomer;

wherein

each of the first and second polypeptides has at least 95% sequence identity to the sequence of DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRDKLTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 49),

each of the third and fourth polypeptides has at least 95% sequence identity to the sequence of DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPSRDELTKNQVSLSCAVDGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 48),

B and B' combine to form a first Fc domain, A and the fifth Fc domain monomer combine to form a second Fc domain, and A' and the sixth Fc domain monomer combine to form a third Fc domain,

each of B and B' comprises the mutations D399K and K409D, each of A and A' comprises the mutations S354C, T366W, and E357K, and each of the fifth and sixth Fc domain monomers comprises the mutations Y349C, T366S, L368A, Y407V, and K370D,

each of L and L' comprises 12-30 glycines, and

each of the first, second, third, and fourth polypeptides lack a C-terminal lysine.

16. The cell culture medium of claim 15, wherein the substantially homogenous population of the Fc construct is at least 85% homogenous.

17. A method of preparing a cell culture medium comprising a substantially homogenous population of an Fc construct of any one of claims 1-11, the method comprising:

a) providing host cells in a cell culture medium, wherein the cells comprise polynucleotides encoding each of the first, second, third, and fourth polypeptides of claim 1;

b) expressing the polypeptides in the host cells under conditions that allow for the formation of the Fc construct and secretion into the cell culture medium; and

c) collecting the cell culture medium.

18. The method of claim 17, wherein the substantially homogenous population of the Fc construct is at least 85% homogenous.

19. The Fc construct of claim 1, wherein each of the first and second polypeptides has at least 97% sequence identity to the sequence of DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRDKLTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 49),

each of the third and fourth polypeptides has at least 97% sequence identity to the sequence of DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPSRDELTKNQVSLSCAVDGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 48).