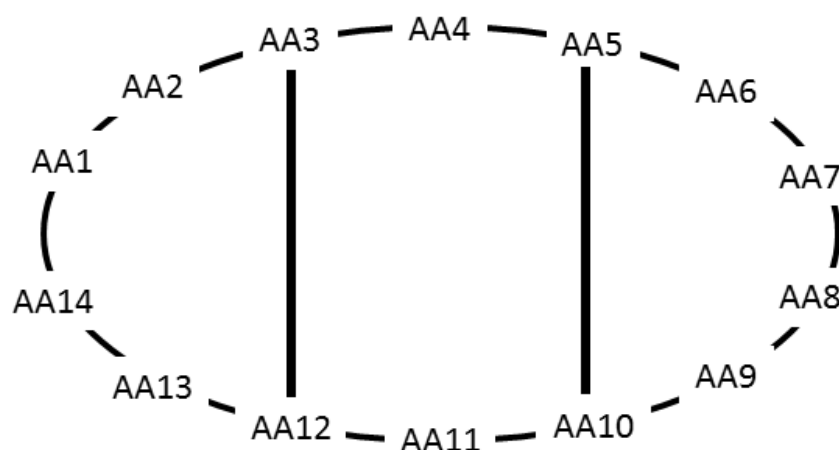


CLAIMS

What is claimed is:

1. A cyclic peptide consisting of 14 amino acids and having the following structure:



wherein AA3 and AA12 are cysteines joined by a disulfide bond, AA5 and AA10 are cysteines joined by a disulfide bond, AA4 is serine or a first hydrophobic amino acid, AA11 is serine or a second hydrophobic acid, AA6 is arginine, AA7 is arginine, AA8 is arginine, and wherein the cyclic peptide comprises five arginine residues that provide a positively charged content of at least about 36% at physiological pH.

2. The cyclic peptide of claim 1, wherein the first hydrophobic amino acid and the second hydrophobic amino acid are selected from the group consisting of leucine and isoleucine.
3. The cyclic peptide of claim 1 or 2, wherein AA1 is glycine.
4. The cyclic peptide of any one of claims 1 to 3, wherein AA2 is a third hydrophobic amino acid.
5. The cyclic peptide of claim 4, wherein the third hydrophobic amino acid is valine or leucine.
6. The cyclic peptide of any one of claims 1 to 5, wherein AA9 is a fourth hydrophobic amino acid.

7. The cyclic peptide of claim 6, wherein the fourth hydrophobic amino acid is valine or phenylalanine.
8. The cyclic peptide of any one of claims 1 to 7, wherein AA13 is arginine.
9. The cyclic peptide of any one of claims 1 to 8, wherein AA14 is arginine.
10. The cyclic peptide of any one of claims 1 to 9, wherein AA4 is not alanine.
11. The cyclic peptide of any one of claims 1 to 10, wherein AA11 is not alanine.
12. The cyclic peptide of any one of claims 1 to ~~12~~11, wherein the cyclic peptide is an analog of a θ -defensin, and wherein the cyclic peptide provides improved survival when applied systemically in a murine disseminated candidiasis model relative to the θ -defensin.
13. The cyclic peptide of any one of claims 1 to 12, wherein the cyclic peptide provides a biphasic response on application to a murine model of disseminated candidiasis, wherein the biphasic response comprises a first phase of mobilization of host effector cells having antifungal activity and a second phase of moderation of host inflammatory response.
14. The cyclic peptide of any one of claims 1 to 13, wherein the cyclic peptide has a TACE inhibiting activity.
15. The cyclic peptide of any one of claims 1 to 14, wherein the cyclic peptide suppresses at least one of expression, processing, and release of TNF.
16. The cyclic peptide of any one of the claims 1 to 15, wherein the cyclic peptide retains activity following exposure to environmental extremes of temperature, low pH, freezing and/or thawing, and dissolution in a biological matrix.
17. The cyclic peptide of claim 16, wherein the biological matrix is selected from the group consisting of blood, plasma, and serum.
18. The cyclic peptide of any one of the claims 1 to 17, wherein the cyclic peptide is non-immunogenic at doses effective to treat disseminated fungal infection.

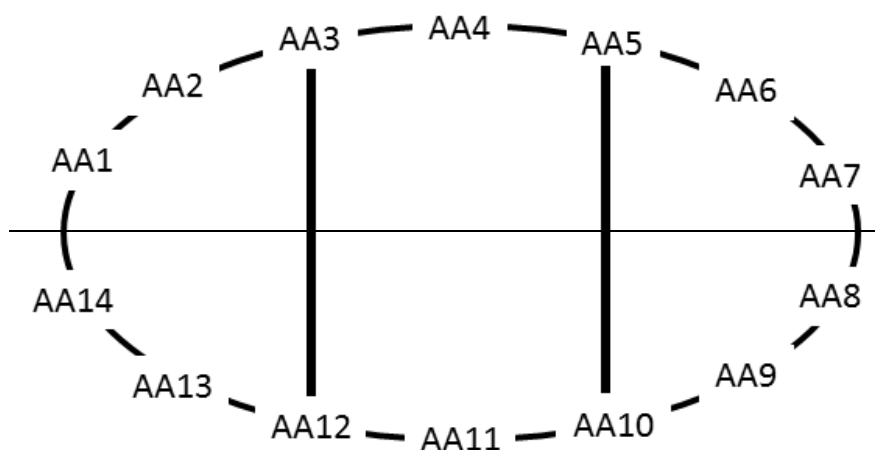
19. The cyclic peptide of any one of the claims 1 to 18, wherein the cyclic peptide activates a host immune system to enhance host clearance of pathogens.

20. The cyclic peptide of any one of the claims 1 to 19, wherein the cyclic peptide is characterized by an activity that modulates inflammation to enhance disease resolution and survival at doses effective to treat disseminated fungal infection.

~~21. A method of treating or preventing disseminated fungal infection and associated septic shock, comprising:~~

~~identifying an individual in need of treatment for disseminated fungal infection; and~~

~~administering a cyclic peptide of an animal at risk of septic shock, wherein the cyclic peptide has the following structure:~~



~~wherein AA3 and AA12 are cysteines joined by a disulfide bond, AA5 and AA10 are cysteines joined by a disulfide bond, AA4 is serine or a first hydrophobic amino acid, AA11 is serine or a second hydrophobic acid, AA6 is arginine, AA7 is arginine, AA8 is arginine, and wherein the cyclic peptide comprises five arginine residues that provide a positively charged content of at least about 36% at physiological pH.~~

~~22. The method of claim 20, are selected from the group consisting of leucine and isoleucine.~~

~~23. The method of claim 21 or 22, wherein AA1 is glycine.~~

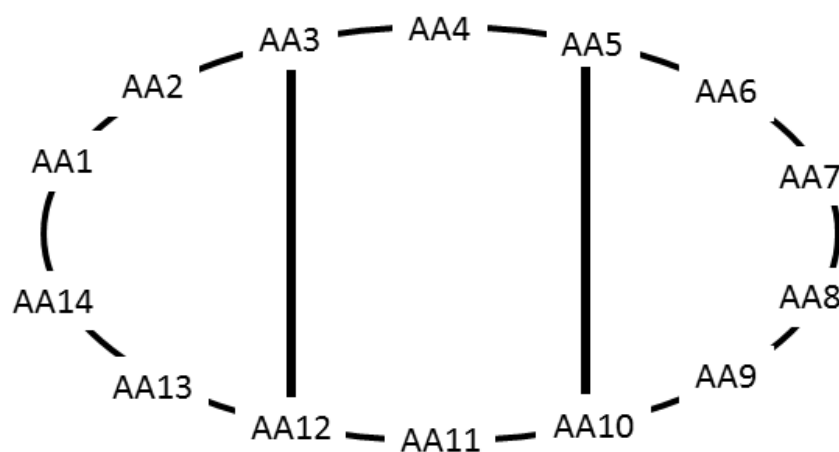
~~24. The method of one of claims 21 to 23, wherein AA2 is a third hydrophobic amino acid.~~

25. The method of claim 24, wherein the third hydrophobic amino acid is leucine, isoleucine, or serine.
26. The method of one of claims 21 to 25, wherein AA9 is a fourth hydrophobic amino acid.
27. The method of claim 26, wherein the fourth hydrophobic amino acid is valine or phenylalanine.
28. The method of one of claims 21 to 27, wherein AA13 is arginine.
29. The method of one of claims 21 to 28, wherein AA14 is arginine.
30. The method of one of claims 21 to 29, wherein AA4 is not alanine.
31. The method of one of claims 21 to 30, wherein AA11 is not alanine.
32. The method of one of claims 21 to 31, wherein the cyclic peptide is an analog of a θ -defensin, and wherein the cyclic peptide provides improved survival when applied systemically in a murine model of disseminated candidiasis relative to the θ -defensin.
33. The method of one of claims 21 to 32, wherein the method provides a biphasic response on application to a murine model of disseminated candidiasis, wherein the biphasic response comprises a first phase of mobilization of host effector cells having antifungal activity and a second phase of moderation of host inflammatory response.
34. The method of one of claims 21 to 33, wherein the method inhibits TACE activity.
35. The method of one of claims 21 to 35, wherein the method suppresses at least one of expression, processing, and release of a proinflammatory cytokine.
36. The method of one of claims 21 to 36, wherein the cyclic peptide retains activity following exposure to environmental extremes of temperature, low pH, freezing and/or thawing, and dissolution in a biological matrix.
37. The method of claim 36, wherein the biological matrix is selected from the group consisting of blood, plasma, and serum.

~~38. The method of one of claims 21 to 38, wherein the cyclic peptide is non-immunogenic at doses effective to treat or prevent disseminated fungal infection.~~

~~39. The method of one of claims 21 to 38, wherein the cyclic peptide activates a host immune system to enhance host clearance of pathogens.~~

~~40~~21. Use of a cyclic peptide for use in the treatment or prevention of ~~in treating or preventing~~ disseminated fungal disease and associated septic shock, wherein the cyclic peptide has the following covalent structure schematic:



wherein AA3 and AA12 are cysteines joined by a disulfide bond, AA5 and AA10 are cysteines joined by a disulfide bond, AA4 is serine or a first hydrophobic amino acid, AA11 is serine or a second hydrophobic acid, AA6 is arginine, AA7 is arginine, AA8 is arginine, and wherein the cyclic peptide comprises five arginine residues that provide a positively charged content of at least about 36% at physiological pH.

~~41~~22. The cyclic peptide use of claim ~~40~~21, wherein the first hydrophobic amino acid and the second hydrophobic amino acid are selected from the group consisting of leucine and isoleucine.

~~42~~23. The cyclic peptide use of claim ~~40~~21 or ~~41~~22, wherein AA1 is glycine.

~~43~~24. The cyclic peptide use of any one of claims ~~40~~21 to ~~42~~23, wherein AA2 is a third hydrophobic amino acid.

~~44~~25. The cyclic peptide ~~use~~-of claim ~~43~~24, wherein the third hydrophobic amino acid is leucine, isoleucine, or serine.

~~45~~26. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~44~~25, wherein AA9 is a fourth hydrophobic amino acid.

~~46~~27. The cyclic peptide ~~use~~-of claim ~~45~~26, wherein the fourth hydrophobic amino acid is valine or phenylalanine.

~~47~~28. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~46~~27, wherein AA13 is arginine.

~~48~~29. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~47~~28, wherein AA14 is arginine.

~~49~~30. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~48~~29, wherein AA4 is not alanine.

~~50~~31. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~49-30~~ wherein AA11 is not alanine.

~~51~~32. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~50~~31, wherein the cyclic peptide is an analog of a θ -defensin, and wherein the cyclic peptide provides improved survival when applied systemically in a murine model of disseminated candidiasis relative to the θ -defensin.

~~52~~33. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~51~~32, wherein the cyclic peptide provides a biphasic response on application to a murine model of disseminated candidiasis, wherein the biphasic response comprises a first phase of recruitment of host effector cells having antimicrobial activity and a second phase of moderation of host inflammatory response.

~~53~~34. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~52~~33, wherein the cyclic peptide has a TACE inhibiting activity.

~~54~~35. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~53~~34, wherein the cyclic peptide suppresses at least one of expression, processing, and release of a proinflammatory cytokine.

~~55~~36. The cyclic peptide ~~use~~-of any one of claims ~~40-21~~ to ~~54~~35, wherein the cyclic peptide retains activity following exposure to environmental extremes of temperature, low pH, freezing and/or thawing, and dissolution in a biological matrix.

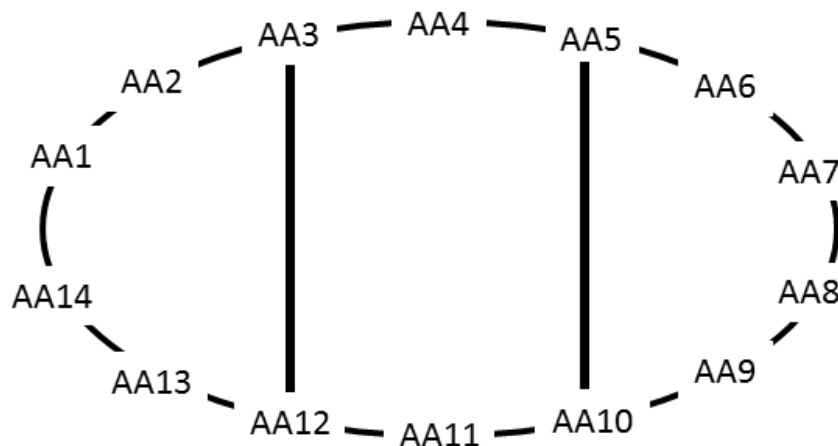
5637. The cyclic peptide use of claim 5536, wherein the biological matrix is selected from the group consisting of blood, plasma, and serum.

5738. The cyclic peptide use of any one of claims 40-21 to 5637, wherein the cyclic peptide is non-immunogenic at doses effective to treat or prevent disseminated fungal disease.

5839. The cyclic peptide use of any one of claims 40-21 to 5738, wherein the cyclic peptide activates a host immune system to enhance host clearance of pathogens.

5940. The cyclic peptide use of any one of claims 40-21 to 5839 wherein the cyclic peptide is characterized by an activity that modulates inflammation to enhance disease resolution and survival at doses effective to treat or prevent disseminated fungal disease.

6041. Use of a cyclic peptide in the manufacture preparation of a medicament for the treatment or prevention of ~~that is effective in treating or preventing~~ disseminated fungal disease and associated septic shock, wherein the cyclic peptide has the following covalent structure schematic:



wherein AA3 and AA12 are cysteines joined by a disulfide bond, AA5 and AA10 are cysteines joined by a disulfide bond, AA4 is serine or a first hydrophobic amino acid, AA11 is serine or a second hydrophobic acid, AA6 is arginine, AA7 is arginine, AA8 is arginine, and wherein the cyclic peptide has four arginine residues that provide a positively charged content of about 36% at physiological pH.

~~61~~42. The use of claim ~~60~~41, wherein the first hydrophobic amino acid and the second hydrophobic amino acid are selected from the group consisting of leucine and isoleucine.

~~62~~43. The use of claim ~~60~~41 or ~~61~~42, wherein AA1 is glycine.

~~63~~44. The use of any one of claims ~~60~~41 to ~~62~~43, wherein AA2 is a third hydrophobic amino acid.

~~64~~45. The use of claim ~~63~~44, wherein the third hydrophobic amino acid is valine or leucine.

~~65~~46. The use of any one of claims ~~60~~41 to ~~64~~45, wherein AA9 is a fourth hydrophobic amino acid.

~~66~~47. The use of claim ~~65~~46, wherein the fourth hydrophobic amino acid is valine or phenylalanine.

~~67~~48. The use of any one of claims ~~60~~41 to ~~66~~47, wherein AA13 is arginine.

~~68~~49. The use of any one of claims ~~60~~41 to ~~67~~48, wherein AA14 is arginine.

~~69~~50. The use of any one of claims ~~60~~41 to ~~68~~49, wherein AA4 is not alanine.

~~70~~51. The use of any one of claims ~~60~~41 to ~~69~~50 wherein AA11 is not alanine.

~~71~~52. The use of any one of claims ~~60~~41 to ~~70~~51, wherein the cyclic peptide is an analog of a θ -defensin, and wherein the cyclic peptide provides improved survival when applied systemically in a murine sepsis model relative to the θ -defensin.

~~72~~53. The use of any one of claims ~~60~~41 to ~~71~~52, wherein the cyclic peptide provides a biphasic response on application to a murine model of disseminated candidiasis, wherein the biphasic response comprises a first phase of recruitment of host effector cells having antimicrobial activity and a second phase of moderation of host inflammatory response.

~~73~~54. The use of any one of claims ~~60~~41 to ~~72~~53, wherein the cyclic peptide has a TACE inhibiting activity.

~~74~~55. The use of any one of claims ~~60-41~~ to ~~73~~54, wherein the cyclic peptide suppresses at least one of expression, processing, and release of a proinflammatory cytokine.

~~75~~56. The use of any one of claims ~~60-41~~ to ~~74~~55, wherein the cyclic peptide retains activity following exposure to environmental extremes of temperature, low pH, freezing and/or thawing, and dissolution in a biological matrix.

~~76~~57. The use of claim ~~75~~56, wherein the biological matrix is selected from the group consisting of blood, plasma, and serum.

~~77~~58. The use of any one of claims ~~60-41~~ to ~~76~~57, wherein the cyclic peptide is non-immunogenic at doses effective to treat or prevent disseminated fungal disease.

~~78~~59. The use of any one of claims ~~60-41~~ to ~~77~~58, wherein the cyclic peptide activates a host immune system to enhance host clearance of pathogens.

~~79~~60. The use of any one of claims ~~60-41~~ to ~~78~~59 wherein the cyclic peptide is characterized by an activity that modulates inflammation to enhance disease resolution and survival at doses effective to treat or prevent disseminated fungal disease.