CLAIMS

1. A recombinant chimeric arginine deiminase (ADI) comprising a catalytic domain of an ADI protein derived from a first microorganism and an α-helical domain of an ADI protein derived from a second microorganism.

2. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the genera *Mycoplasma, Clostridium, Bacillus, Borrelia, Enterococcus, Streptococcus, Lactobacillus*, and *Giardia*.

3. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the group consisting of *Mycoplasma pneumonia, Mycoplasma hominis, Mycoplasma arginini, Mycoplasma arthritidis, Streptococcus pyogenes, streptococcus pneumonia, Borrelia burgdorferi, Borrelia afzelii, Giardia intestinalis, Clostridium perfringens, Bacillus licheniformis,* and *Enterococcus faecalis*.

4. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the group consisting of *M. arginini, M. arthritidis*, *M. hominis, Mycoplasma pneumonia, Mycoplasma phocicerebrale, Mycoplasma orale, Mycoplasma gateae, Mycoplasma phocidae, Mycoplasma columbinum, Mycoplasma iowae, Mycoplasma crocodyli, Mycoplasma fermentans, Mycoplasma penetrans, Mycoplasma gallisepticum, Mycoplasma alligatoris, Mycoplasma mobile*, and *Mycoplasma capricolum*.

5. The recombinant chimeric ADI of claim 1, wherein the second microorganism optionally differs from the first microorganism and is selected from the genera *Mycoplasma, Clostridium, Bacillus, Borrelia, Enterococcus, Streptococcus, Lactobacillus*, and *Giardia*.

6. The recombinant chimeric ADI of claim 1, wherein the second microorganism optionally differs from the first microorganism and is selected from the group consisting of *Mycoplasma pneumonia, Mycoplasma hominis, Mycoplasma arginini, Mycoplasma arthritidis, Streptococcus pyogenes, streptococcus pneumonia, Borrelia*

burgdorferi, Borrelia afzelii, Giardia intestinalis, Clostridium perfringens, Bacillus licheniformis, and Enterococcus faecalis.

7. The recombinant chimeric ADI of claim 1, wherein the second microorganism optionally differs from the first microorganism and is selected from the group consisting of *M. arginini, M. arthritidis*, *M. hominis, Mycoplasma pneumonia, Mycoplasma phocicerebrale, Mycoplasma orale, Mycoplasma gateae, Mycoplasma phocidae, Mycoplasma columbinum, Mycoplasma iowae, Mycoplasma crocodyli, Mycoplasma fermentans, Mycoplasma penetrans, Mycoplasma gallisepticum, Mycoplasma alligatoris, Mycoplasma mobile,* and *Mycoplasma capricolum*.

8. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the group consisting of *Mycoplasma gallinarum, Mycoplasma iners,* and *Mycoplasma columbinum* and wherein the second microorganism optionally differs from the first microorganism and is selected from the group consisting of *Mycoplasma gallinarum, Mycoplasma iners,* and *Mycoplasma columbinum.*

9. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. arginini* and the second microorganism is *M. arthritidis*.

10. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. arginini* and the second microorganism is *M. hominis.*

11. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. arthritidis* and the second microorganism is *M. arginini.*

12. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. gateae* and the second microorganism is *M. arthritidis.*

13. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. gateae* and the second microorganism is *M. columbinum.*

14. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. gateae* and the second microorganism is *M. phocicerebrale*.

15. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. gateae* and the second microorganism is *M. phocidae*.

16. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocicerebrale* and the second microorganism is *M. alligatoris*.

17. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocicerebrale* and the second microorganism is *M. gateae*.

18. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocicerebrale* and the second microorganism is *M. phocidae*.

19. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocidae* and the second microorganism is *M. alligatoris*.

20. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocidae* and the second microorganism is *M. arthritidis*.

21. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocidae* and the second microorganism is *M. columbinum*.

22. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocidae* and the second microorganism is *M. gateae*.

23. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. phocidae* and the second microorganism is *M. phocicerebrale*.

24. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. gallinarum* and the second microorganism is *M. arthritidis*.

25. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. gallinarum* and the second microorganism is *M. iners*.

26. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. iners* and the second microorganism is *M. columbinum*.

27. The recombinant chimeric ADI of claim 1, wherein the first microorganism is *M. iners* and the second microorganism is *M. gallinarum*.

28. The recombinant chimeric ADI of claim 1, wherein the recombinant chimeric ADI comprises the amino acid sequence set forth in any one of SEQ ID NOs:4-13 or 22-59 or a variant having at least 90% identity to any one of SEQ ID NOs:4-13 or 22-59.

29. The recombinant chimeric ADI of any one of the preceding claims, wherein the recombinant chimeric ADI has been modified to remove at least one pegylation site.

30. The recombinant chimeric ADI of any one of the preceding claims, wherein at least one lysine residue has been modified by an amino acid substitution.

31. The recombinant chimeric ADI of claim 30, wherein at least 5 lysine residues have been modified by an amino acid substitution.

32. The recombinant chimeric ADI of claim 30, wherein at least 10 lysine residues have been modified by an amino acid substitution.

33. The recombinant chimeric ADI of claim 30, wherein at least 15 lysine residues have been modified by an amino acid substitution.

34. The recombinant chimeric ADI of claim 30, wherein at least 20 lysine residues have been modified by an amino acid substitution.

35. The recombinant chimeric ADI of claim 30, wherein the recombinant chimeric ADI comprises the amino acid sequence set forth in any one of SEQ ID NOs:10-13.

36. The recombinant chimeric ADI of any one of the preceding claims covalently bonded via a biocompatible linker to polyethylene glycol.

37. The recombinant chimeric ADI of claim 30, wherein the arginine deiminase is covalently bonded to more than one polyethylene glycol molecule.

38. The recombinant chimeric ADI of claim 30, wherein the arginine deiminase is covalently bonded to about 1 to about 10 polyethylene glycol molecules.

39. The recombinant chimeric ADI of claim 30, wherein the arginine deiminase is covalently bonded to 5±3 PEG molecules.

40. The recombinant chimeric ADI of claim 30, wherein the PEG molecules are straight chain or branch chain PEG molecules.

41. The recombinant chimeric ADI of claim 30, wherein the polyethylene glycol has a total weight average molecular weight of from about 1,000 to about 40,000.

42. The recombinant chimeric ADI of claim 30, wherein the polyethylene glycol has a total weight average molecular weight of from about 10,000 to about 30,000.

43. The recombinant chimeric ADI of claim 30, wherein the biocompatible linker comprises a succinyl group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group, a methylene group, or a combination thereof.

44. The recombinant chimeric ADI of claim 30, wherein the source of the succinyl group is succinimidyl succinate.

45. A polynucleotide encoding the recombinant chimeric ADI of any one of the preceding claims.

46. A vector comprising the polynucleotide of claim 45.

47. An isolated host cell comprising the vector of claim 46.

48. A composition comprising the recombinant chimeric ADI of any one of the preceding claims and a physiologically acceptable carrier.

49. The composition of claim 48, further comprising an autophagy modulator.

50. The composition of claim 49, wherein the autophagy modulator is selected from the group consisting of chloroquine, 3-methyladenine, hydroxychloroquine, bafilomycin A1, 5-amino-4-imidazole carboxamide riboside (AICAR), okadaic acid N6-mercaptopurine riboside, vinblastine, wortmannin, rapamycin, everolimus, metformin, perifosine, resveratrol, and tamoxifen.

51. The composition of claim 48, further comprising a chemotherapeutic agent.

52. The composition of claim 51, wherein the chemotherapeutic agent is selected from the group consisting of docetaxel, carboplatin, cyclophosphamide, gemcitabine, cisplatin, sorafenib, sunitinib and everolimus.

53. A method of treating, ameliorating the symptoms of, or inhibiting the progression of a cancer comprising administering to a patient in need thereof a therapeutically effective amount of the composition of claim 48, thereby treating, ameliorating the symptoms of, or inhibiting the progression of the cancer.

54. The method of claim 53, wherein the cancer is selected from the group consisting of melanoma, pancreatic cancer, prostate cancer, small cell lung cancer, mesothelioma, lymphocytic leukemia, chronic myelogenous leukemia, lymphoma, hepatoma, sarcoma, leukemia, acute myeloid leukemia, relapsed acute myeloid leukemia, breast cancer, ovarian cancer, colorectal cancer, gastric cancer, glioma, glioblastoma multiforme, non-small cell lung cancer (NSCLC), kidney cancer, bladder cancer, uterine cancer, esophageal cancer, brain cancer, head and neck cancers, cervical cancer, testicular cancer, and stomach cancer.

CLAIMS

1. A recombinant chimeric arginine deiminase (ADI) comprising a catalytic domain of an ADI protein derived from a first microorganism and an α-helical domain of an ADI protein derived from a second microorganism which differs from the first microorganism.

2. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the genera *Mycoplasma, Clostridium, Bacillus, Borrelia, Enterococcus, Streptococcus, Lactobacillus*, and *Giardia*, and wherein the second microorganism differs from the first microorganism and is selected from the genera *Mycoplasma, Clostridium, Bacillus, Borrelia, Enterococcus, Streptococcus, Lactobacillus*, and *Giardia*.

3. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the group consisting of *Mycoplasma pneumonia, Mycoplasma hominis, Mycoplasma arginini, Mycoplasma arthritidis, Streptococcus pyogenes, streptococcus pneumonia, Borrelia burgdorferi, Borrelia afzelii, Giardia intestinalis, Clostridium perfringens, Bacillus licheniformis,* and *Enterococcus faecalis.*

4. The recombinant chimeric ADI of claim 1, wherein the first microorganism is selected from the group consisting of *M. arginini, M. arthritidis*, *M. hominis, Mycoplasma pneumonia, Mycoplasma phocicerebrale, Mycoplasma orale, Mycoplasma gateae, Mycoplasma phocidae, Mycoplasma columbinum, Mycoplasma iowae, Mycoplasma crocodyli, Mycoplasma fermentans, Mycoplasma gallinarum, Mycoplasma iners, Mycoplasma penetrans, Mycoplasma gallisepticum, Mycoplasma alligatoris, Mycoplasma mobile,* and *Mycoplasma capricolum.*

5. The recombinant chimeric ADI of claim 1, wherein the second microorganism differs from the first microorganism and is selected from the group consisting of *Mycoplasma pneumonia, Mycoplasma hominis, Mycoplasma arginini, Mycoplasma arthritidis, Streptococcus pyogenes, streptococcus pneumonia, Borrelia burgdorferi, Borrelia afzelii, Giardia intestinalis, Clostridium perfringens, Bacillus licheniformis, and Enterococcus faecalis.*

6. The recombinant chimeric ADI of claim 1, wherein the second microorganism differs from the first microorganism is selected from the group consisting of *M. arginini, M. arthritidis*, *M. hominis, Mycoplasma pneumonia, Mycoplasma phocicerebrale, Mycoplasma orale, Mycoplasma gateae, Mycoplasma phocidae, Mycoplasma columbinum, Mycoplasma iowae, Mycoplasma crocodyli, Mycoplasma fermentans, Mycoplasma gallinarum, Mycoplasma iners, Mycoplasma penetrans, Mycoplasma gallisepticum, Mycoplasma alligatoris, Mycoplasma mobile,* and *Mycoplasma capricolum*.

7. The recombinant chimeric ADI of claim 1, wherein:
the first microorganism is *M. arginini* and the second microorganism is *M. arthritidis*;
the first microorganism is *M. arginini* and the second microorganism is *M. hominis*;
the first microorganism is *M. arthritidis* and the second microorganism is *M. arginini*;
the first microorganism is *M. gateae* and the second microorganism is *M. arthritidis*;
the first microorganism is *M. gateae* and the second microorganism is *M. columbinum*;
the first microorganism is *M. gateae* and the second microorganism is *M. phocicerebrale*;
the first microorganism is *M. gateae* and the second microorganism is *M. phocidae*;
the first microorganism is *M. phocicerebrale* and the second microorganism is *M. arginini*;
the first microorganism is *M. phocicerebrale* and the second microorganism is *M. gateae*;
the first microorganism is *M. phocicerebrale* and the second microorganism is *M. phocicerebrale*;
the first microorganism is *M. phocidae* and the second microorganism is *M. arginini*;
the first microorganism is *M. phocidae* and the second microorganism is *M. arthritidis*;
the first microorganism is *M. phocidae* and the second microorganism is *M. columbinum*;
the first microorganism is *M. phocidae* and the second microorganism is *M. gateae*;
the first microorganism is *M. phocidae* and the second microorganism is *M. phocicerebrale*;
the first microorganism is *M. gallinarum* and the second microorganism is *M. columbinum*;
the first microorganism is *M. gallinarum* and the second microorganism is *M. iners*;
the first microorganism is *M. iners* and the second microorganism is *M. columbinum*; or
the first microorganism is *M. iners* and the second microorganism is *M. gallinarum*.

8. The recombinant chimeric ADI of claim 1, wherein the recombinant chimeric ADI comprises the amino acid sequence set forth in any one of SEQ ID NOs:4-13 or 22-59 or a variant having at least 90% identity to any one of SEQ ID NOs:4-13 or 22-59.

9. The recombinant chimeric ADI of any one of claims 1-8, wherein the recombinant chimeric ADI has been modified to remove at least one pegylation site.

10. The recombinant chimeric ADI of any one of claims 1-8, wherein the recombinant chimeric ADI comprises a number of lysine residues and wherein at least one lysine residue has been modified by an amino acid substitution, or wherein at least 5 lysine residues have been modified by an amino acid substitution, or wherein at least 10 lysine residues have been modified by an amino acid substitution, or wherein at least 15 lysine residues have been modified by an amino acid substitution, or wherein at least 20 lysine residues have been modified by an amino acid substitution.

11. The recombinant chimeric ADI of claim 10, wherein the recombinant chimeric ADI comprises the amino acid sequence set forth in any one of SEQ ID NOs:10-13.

12. The recombinant chimeric ADI of any one of claims 1-11, wherein the recombinant chimeric ADI is covalently bonded via a biocompatible linker to polyethylene glycol.

13. The recombinant chimeric ADI of claim 12, wherein the arginine deiminase is covalently bonded to more than one polyethylene glycol molecule.

14. The recombinant chimeric ADI of claim 12, wherein the arginine deiminase is covalently bonded to about 1 to about 10 polyethylene glycol molecules.

15. The recombinant chimeric ADI of claim 12, wherein the arginine deiminase is covalently bonded to 5±3 PEG molecules.

16. The recombinant chimeric ADI of claim 15, wherein the PEG molecules are straight chain or branch chain PEG molecules.

17. The recombinant chimeric ADI of claim 12, wherein the polyethylene glycol has a total weight average molecular weight of from about 1,000 to about 40,000.

18. The recombinant chimeric ADI of claim 12, wherein the polyethylene glycol has a total weight average molecular weight of from about 10,000 to about 30,000.

19. The recombinant chimeric ADI of claim 12, wherein the biocompatible linker comprises a succinyl group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group, a methylene group, or a combination thereof.

20. The recombinant chimeric ADI of claim 19, wherein the source of the succinyl group is succinimidyl succinate.

21. A polynucleotide encoding the recombinant chimeric of claim 1, or a vector comprising the polynucleotide, or an isolated host cell comprising the vector.

22. A composition comprising the recombinant chimeric ADI of any one of claims 1-20 and a physiologically acceptable carrier.

23. Use of a composition according to claim 22 in the manufacture of a medicament for the treatment of cancer or ameliorating the symptoms of, or inhibiting the progression of cancer.

24. The use according to claim 23, wherein the cancer is selected from the group consisting of melanoma, pancreatic cancer, prostate cancer, small cell lung cancer, mesothelioma, lymphocytic leukemia, chronic myelogenous leukemia, lymphoma, hepatoma, sarcoma, leukemia, acute myeloid leukemia, relapsed acute myeloid leukemia, breast cancer, ovarian cancer, colorectal cancer, gastric cancer, glioma, glioblastoma multiforme, non-small cell lung cancer (NSCLC), kidney cancer, bladder cancer, uterine cancer, esophageal cancer, brain cancer, head and neck cancers, cervical cancer, testicular cancer, and stomach cancer.