USE OF A POLYPEPTIDE AS NEUROPROTECTIVE AGENT

CROSS-REFERENCE

[0001] This application claims priority to the PCT application No. PCT/CN2024/081680 filed on March 14, 2024, the contents of which is herein incorporated by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure provides use of a polypeptide as neuroprotective agent. In particular, provided herein is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of any one of the polypeptides disclosed herein.

BACKGROUNG

[0003] Peripheral neuropathy, often shortened to neuropathy, refers to a common type of conditions that involve damage to the peripheral nervous system, which is a vast communications network which sends signals between the central nervous system and all other parts of the body. Different types of neuropathies may cause different symptoms and affect different nerve functions. Neuropathy has a variety of causes, including underlying conditions such as autoimmune diseases, tumors, trauma, infections, metabolic problems, genetic causes, and exposure to toxins or medications such as chemotherapeutic agents or dietary supplements at high dose. For example, diabetic peripheral neuropathy (DPN) is a common complication of diabetes: more than half of the diabetic population will develop DPN during the course of the disease. Chemotherapy-induced peripheral neuropathy (CIPN) is a significant side effect of chemotherapy that limits the dose and potential effectiveness of many first-line agents used in cancer treatment.

[0004] Peripheral neuropathy is often accompanied by nerve injury, which can affect nerve cells, nerve fibers, nerve conduction, etc. Although the pathophysiology of peripheral nerve injury has been extensively studied, finding treatments that significantly improve post-injury neurogenesis, neurite formation, and neuroprotection has been a long-lasting elusive goal. Furthermore, despite the widespread prevalence of peripheral neuropathy, there still remains an unmet need in the medical community for drugs that effectively combat peripheral neuropathy or nerve injury associated therewith.

SUMMARY

[0005] The present disclosure provides polypeptides for use in neuroprotection. Specifically, the present disclosure provides use of the polypeptides as neuroprotective agent, inter alia, a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof using any one of the polypeptides disclosed herein. More specifically, the present disclosure provides a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, improving nerve

conduction velocity in a subject in need thereof, increasing intraepidermal nerve fiber density (IEFND) in a subject in need thereof, or any combination thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), or a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof ("an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), and a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), and a polypeptide having at least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof" are sometimes collectively called "the polypeptides of the present disclosure" or "active ingredients" hereinafter).

[0006] In one aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

[0007] In one aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0008] In one aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0009] In one aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0010] In one aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0011] In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 1, X comprises a sequence having at least 95% identity with SEQ ID NO: 1, or X comprises a sequence of SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence of SEQ ID NO: 1. In some embodiments, at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 81-83.

[0012] In some embodiments, Y comprises a total number of Cysteine (C) of less than 4, Y comprises a total number of Cysteine (C) of less than 3, or Y comprises a total number of Cysteine (C) of less than 2. In some embodiments, Y comprises a total number of Cysteine (C) of less than 4. In some embodiments, Y comprises a total number of Cysteine (C) of less than 3. In some embodiments, Y comprises a total number of Cysteine (C) of less than 2. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8. In some embodiments, the total number of hydrophobic amino acids in Y is more than 12. In some embodiments, the total number of hydrophobic amino acids in Y is more than 15. In some embodiments, a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85, or Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85.

[0013] In some embodiments, the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95.

[0014] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected

from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0015] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

[0016] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0017] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0018] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0019] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0020] In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 1, X comprises a sequence having at least 95% identity with SEQ ID NO: 1, or X comprises a sequence of SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence of SEQ ID NO: 1. In some embodiments, at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H.

[0021] In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8. In some embodiments, the total number of hydrophobic amino acids in Y is more than 12. In some embodiments, the total number of hydrophobic amino acids in Y is more than 15. In some embodiments, a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18, or Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID

NOs: 16-18. In some embodiments, Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18.

[0022] In some embodiments, the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 42-44.

[0023] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine,

vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0024] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

[0025] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0026] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0027] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0028] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0029] In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, Y comprises a sequence having at least 95% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 95% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence of SEQ ID NO: 2. In some embodiments, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0030] In some embodiments, wherein the total number of H, R, K, D, Q, N and E in X is less than 30, the total number of H, R, K, D, Q, N and E in X is less than 25, or the total number of H, R, K, D, Q, N and E in X is less than 20. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 30. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 25. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 20. In some embodiments, a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 15. In some embodiments, a total number of hydrophilic amino acids in X is more than 20. In some embodiments, a total number of hydrophilic amino acids in X is more than 25. In some embodiments, a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, the total number of hydrophobic amino acids in X is no more than 10. In some embodiments, X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 23-27, or X comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 23-27.

[0031] In some embodiments, the polypeptide comprises a sequence having at least 90% identity with SEQ ID NOs: 49-53.

[0032] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is

associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest

pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0033] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

[0034] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0035] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0036] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0037] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0038] In some embodiments, X comprises a sequence having at most 80% identity with SEQ ID NO: 1, X comprises a sequence having at most 70% identity with SEQ ID NO: 1, or X comprises a sequence having at most 50% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at most 80% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at most 70% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at most 50% identity with SEQ ID NO: 1. In some embodiments, a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10. In some embodiments, a total number of hydrophilic amino acids in X is

more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 15. In some embodiments, a total number of hydrophilic amino acids in X is more than 20. In some embodiments, a total number of hydrophilic amino acids in X is more than 25. In some embodiments, a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, the total number of hydrophobic amino acids in X is no more than 10. In some embodiments, X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs:19-22 and 76-79, or X comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 19-22 and 76-79. In some embodiments, X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs:19-22 and 76-79. In some embodiments, X comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 19-22 and 76-79.

[0039] In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, Y comprises a sequence having at least 95% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 95% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence of SEQ ID NO: 2. In some embodiments, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0040] In some embodiments, the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs:45-48 and 86-89.

[0041] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected

from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0042] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

[0043] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0044] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0045] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0046] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0047] In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 1, X comprises a sequence having at least 95% identity with SEQ ID NO: 1, or X comprises a sequence of SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence of SEQ ID NO: 1. In some embodiments, at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 80% identity with SEQ ID NO: 96, X comprises a sequence having at least 90% identity with SEQ ID NO: 96, X comprises a sequence having at least 95% identity with SEQ ID NO: 96, or X comprises a sequence of SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 80% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 95% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence of SEQ ID NO: 96.

[0048] In some embodiments, Y comprises 10 to 25 amino acids, Y comprises 10 to 20 amino acids, or Y comprises 10 to 15 amino acids. In some embodiments, Y comprises 10 to 25 amino acids. In some embodiments, Y comprises 10 to 20 amino acids. In some embodiments, Y comprises 10 to 15 amino acids.

[0049] In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 97-103, Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 97-103, or Y comprises a sequence that is any one selected from

SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence that is any one selected from SEQ ID NOs: 97-103.

[0050] In some embodiments, the polypeptide comprises a sequence having at least 90% identity with any of SEQ ID NOs: 53-56 and 104-110.

[0051] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected

from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0052] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

[0053] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0054] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0055] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0056] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0057] In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1 and/or X comprises a sequence having at most 95% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X comprises a sequence having at most 95% identity with SEQ ID NO: 1. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30 and/or a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30. In some embodiments, a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, X comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 80-83, X comprises a sequence that is any one selected from SEQ ID NOs: 80-83, or X is a sequence that is any one selected from SEQ ID NOs: 80-83. In some embodiments, X comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X comprises a sequence that is any one selected from SEQ ID NOs: 80-83. In some embodiments, X is a sequence that is any one selected from SEQ ID NOs: 80-83.

[0058] In some embodiments, Y comprises a sequence having at least 80% identity with SEQ ID NO: 2 and/or Y comprises a sequence having at most 95% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 80% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 95% identity with SEQ ID NO: 2. In some embodiments, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in Y is more than 10 and/or a total number of W, Y, F, M, L, I, and V in Y is no more than 20. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in Y is more than 10. In some embodiments, a total number of W, Y, F, M, L, I, and V in Y is no more than 20. In some embodiments, Y comprises a sequence having at least 80% identity with SEQ ID NO: 3, Y comprises a sequence of SEQ ID NO: 3, or Y is a sequence of SEQ ID NO: 3. In some embodiments, Y comprises a sequence having at least 80% identity with SEQ ID NO: 3. In some embodiments, Y comprises a sequence of SEQ ID NO: 3. In some embodiments, Y is a sequence of SEQ ID NO: 3.

[0059] In some embodiments, the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 90-93, the artificial polypeptide comprises a sequence that is any one selected from SEQ ID NOs: 90-93, or the artificial polypeptide is a sequence that is any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide comprises a sequence that is any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide is a sequence that is any one selected from SEQ ID NOs: 90-93.

[0060] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some

embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0061] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

[0062] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0063] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0064] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0065] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0066] In some embodiments, the amino acid insertions are located at the N-terminal of X and/or the inserted amino acid is M. In some embodiments, the amino acid insertions are located at the N-terminal of X. In some embodiments, the inserted amino acid is M.

[0067] In some embodiments, at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H and/or at most 60% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, a total number of E or D in X is at least 8 and/or a total number of E or D in X is at most 15. In some embodiments, a total number of E or D in X is at least 8. In some embodiments, a total number of E or D in X is at most 15. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30 and/or a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30. In some embodiments, a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, X comprises a sequence having at least 80% identity with SEQ ID NO: 96, X comprises a sequence of SEQ ID NO: 96, or X is a sequence of SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 80% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence of SEQ ID NO: 96. In some embodiments, X is a sequence of SEQ ID NO: 96.

[0068] In some embodiments, Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations relative to SEQ ID NO: 2 and optionally the at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations are located at the C-terminal of Y. In some embodiments, Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations relative to SEQ ID NO: 2. In some embodiments, the at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations are located at the C-terminal of Y. In some embodiments, Y comprises 15 to 25 amino acids, Y comprises 18 to 25 amino acids, or Y comprises 20 to 25 amino acids. In some embodiments, Y comprises 15 to 25 amino acids. In some embodiments, Y comprises 18 to 25 amino acids. In some embodiments, Y comprises 20 to 25 amino acids. In some embodiments, 40-65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in Y is no more than 10 and/or a total number of W, Y, F, M, L, I, and V in Y is no more than 15. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in Y is no more than 10. In some embodiments, a total number of W, Y, F, M, L, I, and V in Y is no more than 15. In some embodiments, Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103, Y comprises a sequence that is any one selected from SEQ ID NOs: 97-103, or Y is a sequence that is any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence that is any one selected from SEQ ID NOs: 97-103. In some embodiments, Y is a sequence that is any one selected from SEQ ID NOs: 97-103.

[0069] In some embodiments, the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 104-110, the artificial polypeptide comprises a sequence that is any one selected from SEQ ID NOs: 104-110, or the artificial polypeptide is a sequence that is any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide comprises a sequence that is any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide is a sequence that is any one selected from SEQ ID NOs: 104-110.

[0070] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin,

satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0071] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I),

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0072] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0073] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0074] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0075] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0076] In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

[0077] In some embodiments, Y comprises a total number of Cysteine (C) of less than 4, or Y comprises a total number of Cysteine (C) of less than 3. In some embodiments, Y comprises a total number of Cysteine (C) of less than 4. In some embodiments, Y comprises a total number of Cysteine (C) of less than 3. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8. In some embodiments, the total number of hydrophobic amino acids in Y is more than 12. In some embodiments, the total number of hydrophobic amino acids in Y is more than 15. In some embodiments, a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85, or Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85.

[0078] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition,

compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers

and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0079] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II),

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0080] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0081] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0082] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0083] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0084] In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H. In some

embodiments, at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

[0085] In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, a total number of hydrophobic amino acids in Y is more than 8. In some embodiments, the total number of hydrophobic amino acids in Y is more than 12. In some embodiments, the total number of hydrophobic amino acids in Y is more than 15. In some embodiments, a total number of hydrophilic amino acids in Y is no more than 5. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18, or Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18.

[0086] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor

is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0087] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III),

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0088] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0089] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0090] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0091] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0092] In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 30, the total number of H, R, K, D, Q, N and E in X is less than 25, or the total number of H, R, K, D, Q, N and E in X is less than 20. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 30. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 25. In some embodiments, the total number of H, R, K, D, Q, N and E in X is less than 20. In some embodiments, a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 15. In some embodiments, a total number of hydrophilic amino acids in X is more than 20. In some embodiments, a total number of hydrophilic amino acids in X is more than 25. In some embodiments,

a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, the total number of hydrophobic amino acids in X is no more than 10.

[0093] In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence of SEQ ID NO: 2. In some embodiments, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0094] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the

taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0095] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV),

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0096] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0097] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0098] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0099] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0100] In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 10. In some embodiments, a total number of hydrophilic amino acids in X is more than 15. In some embodiments, a total number of hydrophilic amino acids in X is more than 20. In some embodiments, a total number of hydrophilic amino acids in X is more than 25. In some embodiments, a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, the total number of hydrophobic amino acids in X is no more than 10.

[0101] In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence of SEQ ID NO: 2. In some embodiments, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0102] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular

atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject

manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0103] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V),

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0104] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0105] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0106] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0107] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0108] In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

[0109] In some embodiments, Y comprises 10 to 25 amino acids, Y comprises 10 to 20 amino acids, or Y comprises 10 to 15 amino acids. In some embodiments, Y comprises 10 to 25 amino acids. In some embodiments, Y comprises 10 to 20 amino acids. In some embodiments, Y comprises 10 to 15 amino acids.

In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 50% identity with SEQ ID NO: 2.

[0110] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the

taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0111] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0112] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0113] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0114] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0115] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0116] In some embodiments, the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof, the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, the polypeptide is a polypeptide of any one of SEQ ID NOs: 28 and 62-74, or the polypeptide is a polypeptide of SEQ ID NO: 28. In some embodiments, the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof. In some embodiments, the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74. In some embodiments, the polypeptide is a polypeptide of any one of SEQ ID NOs: 28 and 62-74. In some embodiments, the polypeptide is a polypeptide of SEQ ID NO: 28.

[0117] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one

or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0118] In another aspect, provided is an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), or a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof, for use in preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, improving nerve conduction velocity in a subject in need thereof, increasing intraepidermal nerve fiber density in a subject in need thereof, or any combination thereof.

[0119] In another aspect, provided is use of an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), or a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), or a polypeptide having at

least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof for the preparation of a medicament for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, improving nerve conduction velocity in a subject in need thereof, increasing intraepidermal nerve fiber density in a subject in need thereof, or any combination thereof.

[0120] In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the microtubule inhibitor is one or more selected

from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin. In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain. In some embodiments, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0121] Additional aspects and advantages of the present disclosure will become readily apparent to those skilled in this art from the following detailed description, wherein only illustrative embodiments of the present disclosure are shown and described. As will be realized, the present disclosure is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, all without departing from the disclosure. Accordingly, the description are to be regarded as illustrative in nature, and not as restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

[0122] Various features of this disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0123] Fig. 1 shows the motor conduction velocities of median nerves as measured according to Example 1.

[0124] Fig. 2 shows the change rates of the motor conduction of median nerves as measured according to Example 1.

[0125] Fig. 3 shows the sensory conduction velocities of median nerves as measured according to Example 1.

[0126] Fig. 4 shows the change rates of the sensory conduction of median nerves as measured according to Example 1.

[0127] Fig. 5 shows the motor conduction velocities of tibial nerves as measured according to Example 1.

[0128] Fig. 6 shows the results of conduction velocity tests for tail nerves 2 hours post administration on Day 21 as measured according to Example 2.

[0129] Fig. 7 shows the immunofluorescence staining images of epidermises of the right footpads of mice from various groups (20X) as measured according to Example 2.

[0130] Fig. 8 shows the IEFND values of mice from various groups 2 hours post administration on Day 22 as measured according to Example 2.

INCORPORATION BY REFERENCE

[0131] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

DETAILED DESCRIPTION

DEFINITION

[0132] As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

[0133] As used in the specification and claims, the singular forms "a," "an," and "the" include plural references unless the context clearly dictates otherwise. For example, the term "a cell" includes a plurality of cells, including mixtures thereof.

[0134] As used herein, the terms "comprise", "include", "contain" and variations thereof are intended to mean open-ended transitional phrases that do not exclude the possibilities of additional substances or methods. When such terms are used to describe a certain pharmaceutical composition, formulation, kit, use or method of the present disclosure, it also encompasses the situation that the pharmaceutical composition, formulation, kit, use or method consists of the recited substances or methods. For instance, the expression "the solvents comprise water" also includes the situation wherein the solvents are consisting of water, i.e., the solvents contain water exclusively. In the context of this disclosure, the term "consisting of" is intended to mean a close-ended transitional phrase, which excludes the possibilities of additional substances or methods.

[0135] As used herein, ranges as recited in this disclosure are intended to explicitly disclose each of the endpoints of the range and each integer included in the range, unless otherwise indicated. For example, "X is a moiety comprising 40 to 65 amino acids" means that the number of amino acids in the moiety of X can be 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64 or 65. For another example, "Y is a moiety comprising 10 to 50 amino acids" means that that the number of amino

acids in moiety of Y can be 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50. Additionally, any sub-ranges consisting of these integers are intended to be included within the scope of this disclosure. Accordingly, "X is a moiety comprising 40 to 65 amino acids" is regarded as explicitly disclosing the sub-ranges such as "X is a moiety comprising 41 to 64 amino acids", "X is a moiety comprising 42 to 63 amino acids", "X is a moiety comprising 43 to 62 amino acids", etc.

[0136] The term "about" or "approximately" herein means within an acceptable error range of the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, i.e., the limitations of the measurement system. For example, "about" can mean within 1 or more than 1 standard deviation, per the practice in the art. Alternatively, "about" can mean a range of up to 20%, up to 10%, up to 5%, or up to 1% of a given value. Where particular values are described in the application and claims, unless otherwise stated, the term "about" or "approximately" meaning within an acceptable error range for the particular value should be assumed.

[0137] The term "optional(ly)" means that the subsequently described event of circumstances may or may not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not.

[0138] The terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified, for example, by disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component.

[0139] The term "fragment" as used herein, when applied to a protein, refers to a truncated form of a native biologically active protein that may or may not retain at least a portion of the therapeutic and/or biological activity.

[0140] The term "variant" as used herein, when applied to a protein, refers to a protein with sequence homology to the native biologically active protein that retains at least a portion of the therapeutic and/or biological activity of the biologically active protein. For example, a variant protein may share at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity as compared to the reference biologically active protein.

[0141] As used herein the term "amino acid (AA)" refers to either natural and/or unnatural or synthetic amino acids, including but not limited to glycine and both the D or L optical isomers, and amino acid analogs and peptidomimetics. Standard single or three letter codes are used to designate amino acids.

[0142] The term "natural L-amino acid" means the L optical isomer forms of glycine (G), proline (P), alanine (A), valine (V), leucine (L), isoleucine (I), methionine (M), cysteine (C), phenylalanine (F), tyrosine (Y), tryptophan (W), histidine (H), lysine (K), arginine (R), glutamine (Q), asparagine (N), glutamic acid (E), aspartic acid (D), serine (S), and threonine (T).

[0143] The terms "hydrophilic" and "hydrophobic" refer to the degree of affinity that a substance has with water. A hydrophilic substance has a strong affinity for water, tending to dissolve in, mix with, or be

wetted by water, while a hydrophobic substance substantially lacks affinity for water, tending to repel and not absorb water and tending not to dissolve in or mix with or be wetted by water. Amino acids can be characterized based on their hydrophobicity. Examples of "hydrophilic amino acids" are arginine, lysine, threonine, alanine, asparagine, and glutamine. Of particular interest are the hydrophilic amino acids aspartate, glutamate, serine, and glycine. In some embodiments, "hydrophilic amino acids" refers to arginine, lysine, threonine, alanine, asparagine, glutamine, aspartate, glutamate, serine, and glycine. Examples of "hydrophobic amino acids" are tryptophan, tyrosine, phenylalanine, methionine, leucine, isoleucine, and valine. In some embodiments, "hydrophobic amino acids" refers to tryptophan, tyrosine, phenylalanine, methionine, leucine, isoleucine, and valine.

[0144] A "host cell" includes an individual cell or cell culture which can be or has been a recipient for the subject vectors. Host cells include progeny of a single host cell. The progeny may not necessarily be completely identical (in morphology or in genomic of total DNA complement) to the original parent cell.

[0145] "Conjugated", "linked," "fused," and "fusion" are used interchangeably herein. These terms refer to the joining together of two more chemical elements or components, by whatever means including chemical conjugation or recombinant means.

[0146] The terms "polynucleotides", "nucleic acids", "nucleotides" and "oligonucleotides" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. Polynucleotides may have any three-dimensional structure, and may perform any function, known or unknown. The following are non-limiting examples of polynucleotides: coding or non-coding regions of a gene or gene fragment, loci (locus) defined from linkage analysis, exons, introns, messenger RNA (mRNA), transfer RNA, ribosomal RNA, ribozymes, cDNA, recombinant polynucleotides, branched polynucleotides, plasmids, vectors, isolated DNA of any sequence, isolated RNA of any sequence, nucleic acid probes, and primers. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. If present, modifications to the nucleotide structure may be imparted before or after assembly of the polymer. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component.

[0147] The term "complement of a polynucleotide" denotes a polynucleotide molecule having a complementary base sequence and reverse orientation as compared to a reference sequence, such that it could hybridize with a reference sequence with complete fidelity.

[0148] The term "recombinant" as applied to a polynucleotide means that the polynucleotide is the product of various combinations of in vitro cloning, restriction and/or ligation steps, and other procedures that result in a construct that can potentially be expressed in a host cell.

[0149] The term "homology" or "homologous" refers to sequence similarity or interchangeability between two or more polynucleotide sequences or two or more polypeptide sequences. When using a program such as BestFit to determine sequence identity, similarity or homology between two different amino acid sequences, the default settings may be used, or an appropriate scoring matrix, such as blosum45 or blosum80, may be selected to optimize identity, similarity or homology scores. Preferably, polynucleotides

that are homologous are those which hybridize under stringent conditions as defined herein and have at least 70%, preferably at least 80%, more preferably at least 90%, more preferably 95%, more preferably 97%, more preferably 98%, and even more preferably 99% sequence identity to those sequences.

[0150] The terms "percent identity" and "% identity", as applied to polynucleotide sequences, refer to the percentage of residue matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps in the sequences being compared in order to optimize alignment between two sequences, and therefore achieve a more meaningful comparison of the two sequences. Percent identity may be measured over the length of an entire defined polynucleotide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polynucleotide sequence, for instance, a fragment of at least 45, at least 60, at least 90, at least 120, at least 150, at least 210 or at least 450 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

[0151] "Percent (%) amino acid sequence identity", with respect to the polypeptide sequences identified herein, is defined as the percentage of amino acid residues in a query sequence that are identical with the amino acid residues of a second, reference polypeptide sequence or a portion thereof, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance, a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

[0152] A "vector" is a nucleic acid molecule, preferably self-replicating in an appropriate host, which transfers an inserted nucleic acid molecule into and/or between host cells. The term includes vectors that function primarily for insertion of DNA or RNA into a cell, replication of vectors that function primarily for the replication of DNA or RNA, and expression vectors that function for transcription and/or translation of the DNA or RNA. Also included are vectors that provide more than one of the above functions. An "expression vector" is a polynucleotide which, when introduced into an appropriate host cell, can be transcribed and translated into a polypeptide(s). An "expression system" usually connotes a suitable host cell comprised of an expression vector that can function to yield a desired expression product.

[0153] The term "physiological conditions" refers to a set of conditions in a living host as well as *in vitro* conditions, including temperature, salt concentration, pH, that mimic those conditions of a living subject. A host of physiologically relevant conditions for use in *in vitro* assays have been established. Generally, a physiological buffer contains a physiological concentration of salt and is adjusted to a neutral pH ranging from about 6.5 to about 7.8, and preferably from about 7.0 to about 7.5. A variety of physiological buffers is listed in Sambrook et al. (1989). Physiologically relevant temperature ranges from about 25 ˚C to about 38 ˚C, and preferably from about 35 ˚C to about 37 ˚C.

[0154] The term "antagonist" as used herein, includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native polypeptide disclosed herein. Methods for identifying antagonists of a polypeptide may comprise contacting a native polypeptide with a candidate antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the native polypeptide. In the context of the present disclosure, antagonists may include proteins, nucleic acids, carbohydrates, antibodies or any other molecules that decrease the effect of a biologically active protein.

[0155] The term "agonist" is used in the broadest sense and includes any molecule that mimics a biological activity of a native polypeptide disclosed herein. Suitable agonist molecules specifically include agonist antibodies or antibody fragments, fragments or amino acid sequence variants of native polypeptides, peptides, small organic molecules, etc. Methods for identifying agonists of a native polypeptide may comprise contacting a native polypeptide with a candidate agonist molecule and measuring a detectable change in one or more biological activities normally associated with the native polypeptide.

[0156] The term "activity" for the purposes herein refers to an action or effect of a component of a fusion protein consistent with that of the corresponding native biologically active protein, wherein "biological activity" refers to an *in vitro* or *in vivo* biological function or effect, including but not limited to receptor binding, antagonist activity, agonist activity, or a cellular or physiologic response.

[0157] As used herein, "treatment" or "treating," "palliating," and "ameliorating" are used interchangeably. These terms refer to an approach for obtaining beneficial or desired results including but not limited to a therapeutic benefit and/or a prophylactic benefit. By "therapeutic benefit" is meant eradication or amelioration of the underlying disorder being treated. Also, a therapeutic benefit is achieved with the eradication or amelioration of one or more of the physiological symptoms associated with the underlying disease condition such that an improvement is observed in the subject, notwithstanding that the subject may still be afflicted with the underlying disorder. For prophylactic benefit, the compositions may be administered to a subject at risk of developing a particular disease condition, or to a subject reporting one or more of the physiological symptoms of a disease, even though a diagnosis of this disease may not have been made.

[0158] The term "therapeutic effect" refers to a physiologic effect, including but not limited to the cure, mitigation, amelioration, or prevention of disease condition in humans or other animals, or to otherwise enhance physical or mental wellbeing of humans or animals, caused by a polypeptide of the present

disclosure. Determination of a therapeutically effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

[0159] The term "effective amount" refers to an amount of a biologically active protein, either alone or as a part of a fusion protein composition, that is capable of having any detectable, beneficial effect on any symptom, aspect, measured parameter or characteristics of a disease state or condition when administered in one or repeated doses to a subject. Such effect need not be absolute to be beneficial. The disease condition can refer to a disorder or a disease.

[0160] The term "pharmaceutically acceptable" refers to those compounds, materials, compositions, formulations or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and other animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0161] The terms "formulation" and "dosage form" are used interchangeably and refer to a pharmaceutical composition that is formulated in accordance with clinical requirements, in a form that can be directly administered to a subject in need thereof for preventive or therapeutic use.

[0162] The term "pharmaceutically acceptable excipient" refers to a pharmaceutically acceptable material, carrier, or vehicle which are used for the preparation of the formulations or dosage forms in accordance with the present disclosure. Each excipient must be "acceptable" in the sense of being compatible with the other ingredients of the formulations or dosage forms and not injurious to the patient.

[0163] The term "subject" "individual" or "patient" as used herein refers to any animals that can be used in the present disclosure, including but not limited to human, primate, rodent, canine, feline, equine, ovine, porcine, and the like.

[0164] The terms "administer", "administered", "administers", "administering" and "dosing" are used interchangeably and are defined as providing a compound, a composition, a formulation and/or a dosage form in accordance with the present disclosure to a subject in need thereof via a route known in the art, including but not limited to oral, buccal, topical, transmucosal, transdermal, rectal, and parenteral routes of administration. In some embodiments, an oral route of administration is used. In some embodiments, a parenteral route of administration, including intravenous, intraarterial, intramuscular, subcutaneous, intraosseous, and intraperitoneal is used. In some embodiments, a topical route of administration is used.

[0165] The term "*in vivo*" as used herein refers to an event that takes place in a subject's body.

[0166] The term "*in vitro*" as used herein refers to an event that takes places outside of a subject's body. In some embodiments, an *in vitro* assay encompasses any assay run outside of a subject assay. *In vitro* assays encompass cell-based assays in which cells alive or dead are employed. *In vitro* assays also encompass a cell-free assay in which no intact cells are employed.

[0167] The term "peripheral neuropathy" as used herein refers to a common type of conditions that involve damage to the peripheral nervous system, which is a vast communications network which sends signals between the central nervous system and all other parts of the body. Damage to the peripheral nervous system may impair sensation, movement, gland function, and/or organ function, depending on the nerves

being affected. Different symptoms may result from peripheral neuropathy affecting motor, sensory, or autonomic nerves.

[0168] The term "nerve injury" as used herein refers to an injury to a nerve. Injury to a nerve can stop signals to and from the brain, and can in turn cause muscles to stop working properly and lead to loss of feeling. Peripheral neuropathy is often accompanied by nerve injury, which can affect nerve cells, nerve fibers, nerve conduction, etc.

[0169] The term "neuroprotection" as used herein refers to the relative preservation of neuronal structure and/or function. The aim of neuroprotection is to prevent or slow progression of disease and secondary injuries by halting or at least slowing the loss of neurons.

[0170] The term "neuroprotective agent" as used herein refers to an agent that has neuroprotective function. Neuroprotective agents are needed in subjects afflicted by clinical conditions in which nerve injury is implicated.

[0171] The term "neuroregeneration" as used herein refers to the regrowth or repair of nervous tissues, cells or cell products, the mechanisms of which may include the generation of new neurons, glia, axons, myelin, or synapses.

[0172] The term "nervous tissue" as used herein refers to the main tissue component of the nervous system. It is composed of neurons, also termed as nerve cells, which receive and transmit impulses, and neuroglia, also termed as glial cells or glia, which assist the propagation of the nerve impulse as well as provide nutrients to the neurons.

[0173] The term "cell damage" as used herein refers to a variety of changes of stress that a cell suffers due to external as well as internal environmental changes.

[0174] The term "inflammatory response" as used herein refers to part of the biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants.

[0175] The term "nerve conduction velocity" as used herein refers to the rate at which nerve signals travel along a nerve or nerve fiber. Usually, it is measured in meters per second (m/s). Impaired nerve conduction velocity is considered a very unique symptom of neuropathy, and medications used for treating neuralgia are generally not used to treat impaired nerve conduction velocity.

[0176] The term "intraepidermal nerve fiber density (IEFND)" as used herein refers to the density of nerves in the outer layer of the skin. IEFND is a measure used to assess the extent of neuropathy. To assess IEFND, the number of nerve fibers in skin biopsy samples is determined. An increase in the number/density of intraepidermal nerve fibers indicates improvement in neuropathy.

[0177] The term "diabetic peripheral neuropathy (DPN)" as used herein refers to a long-term major complication of diabetes mellitus, in which exposure to high blood glucose levels over an extended period of time causes damage to the peripheral nerves going to the arms, hands, legs, and feet.

[0178] The term "chemotherapy-induced peripheral neuropathy (CIPN)" as used herein refers to is a nerve-damaging side effect of antitumor agents in chemotherapy. Antitumor agents can cause injuries to healthy structures, including the peripheral nervous system. CIPN involves various symptoms such as tingling, pain, and numbness in the hands and feet, impairing activities of daily living of the patients.

METHODS OF TREATMENT AND THERAPEUTIC USES

[0179] In one aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

[0180] In one aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0181] In one aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0182] In one aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0183] In one aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I).

[0184] In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 50% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 55% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 60% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 65% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 70% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 75% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 80% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 85% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 90% of which are selected from R, K, N, D, Q, E, and H.

[0185] In some embodiments, X of formula (I) can be a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least

85% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising the sequence of SEQ ID NO: 1. In some embodiments, X is a moiety that is the sequence of SEQ ID NO: 1.

[0186] In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 50% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 55% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 60% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 65% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 70% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 75% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 80% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 85% of which are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (I) can be a hydrophobic moiety, at least 90% of which are selected from I, V, L, F, C, M, and A.

[0187] In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 5. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 5. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 6. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 6. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 7. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 7. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 8. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 8. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 9. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 9. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 10. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 10. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 11. In some embodiments, Y of formula (I) can be a moiety comprising

10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 11. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 12. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 12. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 13. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 13. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 14. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 14. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is 15. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of hydrophobic amino acids of Y is more than 15.

[0188] In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 5. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 5. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 6. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 6. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 7. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 7. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 8. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 8. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 9. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 9. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 10. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 10. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 11. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 11. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 12. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 12. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 13. In some

embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 13. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 14. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 14. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is 15. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of I, V, L, F, C, M, and A of Y is more than 15.

[0189] In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 5. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 5. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 4. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 4. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 3. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 3. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 2. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 2. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 1. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 1. In some embodiments, Y of formula (I) can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 0.

[0190] In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is 5. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is no more than 5. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is 4. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is no more than 4. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is 3. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is no more than 3. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is 2. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is no more than 2. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is 1. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is no more than 1.

[0191] In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is 5. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is no more than 5. In some embodiments, a total number of hydrophilic amino acids in Y of formula (I) is 4. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is no more than 4. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is 3. In some embodiments, a total number of

R, K, N, D, Q, E, and H in Y of formula (I) is no more than 3. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is 2. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is no more than 2. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is 1. In some embodiments, a total number of R, K, N, D, Q, E, and H in Y of formula (I) is no more than 1.

[0192] In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) comprises a sequence of any one selected from SEQ ID NOs: 81-83. In some embodiments of the artificial polypeptide, X of formula (I) is a sequence of any one selected from SEQ ID NOs: 81-83.

[0193] In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) comprises a sequence of any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments of the artificial polypeptide, Y of formula (I) is a sequence of any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85.

[0194] In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-

95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide comprises a sequence of any one of SEQ ID NOs: 29-41, 54-57, 75 and 91-95. In some embodiments of the artificial polypeptide of formula (I), the polypeptide is a sequence of any one of SEQ ID NOs: 29-41, 54-57, 75 and 91-95.

[0195] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

[0196] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0197] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0198] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0199] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II).

[0200] In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 50% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 55% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (I) can be a hydrophilic moiety, at least 60% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 65% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 70% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of (II) can be a hydrophilic moiety, at least 75% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 80% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 85% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (II) can be a hydrophilic moiety, at least 90% of which are selected from R, K, N, D, Q, E, and H.

[0201] In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Arginine (R). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Arginine (R). In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Lysine (K). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Lysine (K). In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Asparagine (N). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Asparagine (N). In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Aspartic Acid (D). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Aspartic Acid (D). In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Glutamine (Q). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Glutamine (Q). In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Glutamic Acid (E). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Glutamic Acid (E). In some embodiments, X of formula (II) can be a hydrophilic moiety comprising one or more Histidine (H). For example, X of formula (II) can be a hydrophilic moiety comprising at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten Histidine (H).

[0202] In some embodiments, X of formula (II) can be a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having

at least 90% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising the sequence of SEQ ID NO: 1. In some embodiments, X is a moiety that is the sequence of SEQ ID NO: 1.

[0203] In some embodiments of the artificial polypeptide of formula (II), Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 55% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 60% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 65% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 75% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 85% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

[0204] In some embodiments of the artificial polypeptide of formula (II), Y comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y comprises a sequence of any one selected from SEQ ID NOs: 16-18. In some embodiments of the artificial polypeptide, Y is a sequence of any one selected from SEQ ID NOs: 16-18.

[0205] In some embodiments of the artificial polypeptide of formula (II), the artificial polypeptide comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence having at least 95% identity with any

one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide comprises a sequence of any one selected from SEQ ID NOs: 42-44. In some embodiments of the artificial polypeptide, the artificial polypeptide is a sequence of any one selected from SEQ ID NOs: 42-44.

[0206] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

[0207] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0208] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0209] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0210] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III).

[0211] In some embodiments, X of formula (III) is hydrophilic moiety, at least 50% of which are selected from H, R, K, D, Q, N and E. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 55% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 60% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 65% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 70% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 75% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 80% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 85% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (III) can be a hydrophilic moiety, at least 90% of which are selected from R, K, N, D, Q, E, and H.

[0212] In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 33. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 32. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 31. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 30. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 29. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 28. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 27. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 26. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 25. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 24. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 23. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 22. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 21. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 20.

[0213] In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 10. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 11. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 12. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 13. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 14. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 15. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 16. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 17. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 18. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 19. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 20. In some embodiments, X of formula (III) is a

moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 21. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 22. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 23. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 24. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 25.

[0214] In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 14. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 13. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 12. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 11. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 10. In some embodiments, X of formula (III) is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 5.

[0215] In some embodiments, X of formula (III) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) comprises a sequence of any one selected from SEQ ID NOs: 23-27. In some embodiments, X of formula (III) is a sequence of any one selected from SEQ ID NOs: 23-27.

[0216] In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 70% identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 75% identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 95%

identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety comprising a sequence of SEQ ID NO: 2. In some embodiments, Y of formula (III) is a moiety that is a sequence of SEQ ID NO: 2.

[0217] In some embodiments, Y of formula (III) is hydrophobic moiety, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 70% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 75% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 80% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 85% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (III) is hydrophobic moiety, at least 90% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0218] In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) comprises a sequence of any one selected from SEQ ID NOs: 49-53. In some embodiments, the artificial polypeptide of formula (III) is a sequence of any one selected from SEQ ID NOs: 49-53.

[0219] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

[0220] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0221] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0222] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0223] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV).

[0224] In some embodiments, X of formula (IV) is a hydrophilic moiety, at least 50% of which are selected from H, R, K, D, Q, N and E. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 55% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 60% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 65% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 70% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 75% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 80% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 85% of which are selected from R, K, N, D, Q, E, and H. In some embodiments, X of formula (IV) can be a hydrophilic moiety, at least 90% of which are selected from R, K, N, D, Q, E, and H.

[0225] In some embodiments, X of formula (IV) comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 10. In some embodiments, X of formula (IV) comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 15. In some embodiments, X of formula (IV) comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 20. In some embodiments, X of formula (IV) comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 25. In some embodiments, X of formula (IV) comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 30. In some embodiments, X of formula (IV) comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 35.

[0226] In some embodiments, X of formula (IV) comprises a sequence having at most 50% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 55% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 60% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 65% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence

having at most 70% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 75% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 80% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 85% identity with SEQ ID NO: 1. In some embodiments, X of formula (IV) comprises a sequence having at most 90% identity with SEQ ID NO: 1.

[0227] In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 70% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 75% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety comprising a sequence of SEQ ID NO: 2. In some embodiments, Y of formula (IV) is a moiety that is a sequence of SEQ ID NO: 2.

[0228] In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 70% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 75% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 80% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 85% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (IV) is hydrophobic moiety, at least 90% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0229] In some embodiments, X of formula (IV) comprises a sequence having at least 70% identity with any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence having at least 75% identity with any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence having at least 80% identity with any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence having at least 85% identity with any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence having at least 90% identity with any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence having at least 95% identity with any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with

any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) comprises a sequence of any one selected from SEQ IDs NO.19-22 and 76-79. In some embodiments, X of formula (IV) is a sequence of any one selected from SEQ IDs NO.19-22 and 76-79.

[0230] In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) comprises a sequence of any one selected from SEQ ID NOs: 45-48 and 86-89. In some embodiments, the artificial polypeptide of formula (IV) is a sequence of any one selected from SEQ ID NOs: 45-48 and 86-89.

[0231] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

[0232] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0233] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0234] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0235] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V).

[0236] In some embodiments, Y of formula (V) comprises 10 to 25 amino acids. In some embodiments, Y comprises 10 to 20 amino acids. In some embodiments, Y comprises 10 to 15 amino acids. In some embodiments, Y comprises 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 amino acids.

[0237] In some embodiments, X of formula (V) can be a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 1. In some embodiments, X is a moiety comprising the sequence of SEQ ID NO: 1. In some embodiments, X is a moiety that is the sequence of SEQ ID NO: 1.

[0238] In some embodiments of the artificial polypeptide of formula (V), at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 55% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 60% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 65% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 70% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 75% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 80% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 85% amino acids of X are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 90% amino acids of X are selected from R, K, N, D, Q, E, and H.

[0239] In some embodiments of the artificial polypeptide of formula (V), X comprises a sequence having at least 70% identity with SEQ ID NO: 96. In some embodiments of the artificial polypeptide of formula (V), X comprises a sequence having at least 75% identity with SEQ ID NO: 96. In some embodiments of the artificial polypeptide of formula (V), X comprises a sequence having at least 80% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 85% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 90% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 95% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 96. In some embodiments, X comprises a sequence of SEQ ID NO: 96. In some embodiments, X is a sequence of SEQ ID NO: 96.

[0240] In some embodiments of the artificial polypeptide of formula (V), Y comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 55% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 60% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 65% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 75% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 80% identity with SEQ ID NO: 2.

In some embodiments, Y comprises a sequence having at most 85% identity with SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

[0241] In some embodiments of the artificial polypeptide of formula (V), Y comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments of the artificial polypeptide of formula (V), Y comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments of the artificial polypeptide of formula (V), Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y comprises a sequence that is any one selected from SEQ ID NOs: 97-103. In some embodiments, Y is a sequence that is any one selected from SEQ ID NOs: 97-103.

[0242] In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) comprises a sequence of any one selected from SEQ ID NOs:53-56 and 104-110. In some embodiments, the artificial polypeptide of formula (V) is a sequence of any one selected from SEQ ID NOs:53-56 and 104-110.

[0243] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

[0244] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0245] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0246] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0247] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI).

[0248] In some embodiments, X of formula (VI) comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at least 75% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at least 95% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at most 95% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at most 90% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at most 85% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at most 80% identity with SEQ ID NO: 1. In some embodiments, X of formula (VI) comprises a sequence having at most 75% identity with SEQ ID NO: 1.

[0249] In some embodiments, Y of formula (VI) is a moiety comprising a sequence having at least 70% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) is a moiety comprising a sequence having at least 75% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) comprises a sequence having at most 95% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) comprises a sequence having at most 90% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) comprises a sequence having at most 85% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI)

comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y of formula (VI) comprises a sequence having at most 75% identity with SEQ ID NO: 2.

[0250] In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 70% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 75% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 80% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 85% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y of formula (VI) is hydrophobic moiety, at least 90% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0251] In some embodiments, X of formula (VI) is a moiety comprising 40 to 65 amino acids, and a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30. In some embodiments, X of formula (VI) is a moiety comprising 40 to 65 amino acids, and a total number of R, K, T, A, N, Q, D, E, S, and G in X is 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40. In some embodiments, X of formula (VI) is a moiety comprising 40 to 65 amino acids, and a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, X of formula (VI) is a moiety comprising 40 to 65 amino acids, and a total number of W, Y, F, M, L, I, and V in X is 19, 18, 17, 16, 15 or 14.

[0252] In some embodiments, Y of formula (VI) is a moiety comprising 10 to 50 amino acids, and a total number of R, K, T, A, N, Q, D, E, S, and G in Y is more than 10. In some embodiments, Y of formula (VI) is a moiety comprising 10 to 50 amino acids, and a total number of R, K, T, A, N, Q, D, E, S, and G in Y is 11, 12, 13, 14 or 15. In some embodiments, Y of formula (VI) is a moiety comprising 10 to 50 amino acids, and a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, Y of formula (VI) is a moiety comprising 10 to 50 amino acids, and a total number of W, Y, F, M, L, I, and V in Y is 19, 18, 17, 16, 15 or 14.

[0253] In some embodiments, X of formula (VI) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 80-83. In some embodiments,

X of formula (VI) comprises a sequence of any one selected from SEQ ID NOs: 80-83. In some embodiments, X of formula (VI) is a sequence of any one selected from SEQ ID NOs: 80-83.

[0254] In some embodiments, Y of formula (VI) comprises a sequence having at least 70% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence having at least 75% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence having at least 80% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence having at least 85% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence having at least 90% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence having at least 95% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 3. In some embodiments, Y of formula (VI) comprises a sequence of SEQ ID NO: 3. In some embodiments, Y of formula (VI) is a sequence of SEQ ID NO: 3.

[0255] In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) comprises a sequence that is any one selected from SEQ ID NOs: 90-93. In some embodiments, the artificial polypeptide of formula (VI) is a sequence that is any one selected from SEQ ID NOs: 90-93.

[0256] In one aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

[0257] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0258] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0259] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0260] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII).

[0261] In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1 amino acid insertion relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has 1 amino acid insertion relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 2 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has 2 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 3 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has 3 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 4 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has 4 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 5 amino acid insertions relative to SEQ ID NO: 1. In some embodiments, X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has 5 amino acid insertions relative to SEQ ID NO: 1.

[0262] In some embodiments, at least 20% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 25% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 35% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 40% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 45% amino acids of X in the mutant

are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 55% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 65% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 70% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 75% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 85% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H.

[0263] In some embodiments, Y is a moiety comprising 10 to 30 amino acids. In some embodiments, Y is a moiety comprising 10 amino acids, 11 amino acids, 12 amino acids, 13 amino acids, 14 amino acids, 15 amino acids, 16 amino acids, 17 amino acids, 18 amino acids, 19 amino acids, 20 amino acids, 21 amino acids, 22 amino acids, 23 amino acids, 24 amino acids, 25 amino acids, 26 amino acids, 27 amino acids, 28 amino acids, 29 amino acids, or 30 amino acids. In some embodiments, Y is a moiety comprising 11 to 29 amino acids. In some embodiments, Y is a moiety comprising 12 to 28 amino acids. In some embodiments, Y is a moiety comprising 13 to 27 amino acids. In some embodiments, Y is a moiety comprising 14 to 26 amino acids. In some embodiments, Y is a moiety comprising 15 to 25 amino acids. In some embodiments, Y comprises 15 to 25 amino acids. In some embodiments, Y comprises 18 to 25 amino acids. In some embodiments, Y comprises 20 to 25 amino acids.

[0264] In some embodiments, Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 15 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 16 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 16 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 17 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 17 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 18 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 18 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 19 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 19 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 20 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 20 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 21 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 21 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 22 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 22 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 23 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 23 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 24 continuous AAs of SEQ ID NO: 2. In some

embodiments, Y comprises a sequence having 24 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having at least 25 continuous AAs of SEQ ID NO: 2. In some embodiments, Y comprises a sequence having 25 continuous AAs of SEQ ID NO: 2.

[0265] In some embodiments, Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations relative to SEQ ID NO: 2. In some embodiments, the at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations are located at the C-terminal of Y. In some embodiments, Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations relative to SEQ ID NO: 2. In some embodiments, the 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations are located at the C-terminal of Y.

[0266] In some embodiments, a total number of E or D in X is at least 8. In some embodiments, a total number of E or D in X is 8. In some embodiments, a total number of E or D in X is at least 9. In some embodiments, a total number of E or D in X is 9. In some embodiments, a total number of E or D in X is at least 10. In some embodiments, a total number of E or D in X is 10. In some embodiments, a total number of E or D in X is at least 11. In some embodiments, a total number of E or D in X is 11. In some embodiments, a total number of E or D in X is at least 12. In some embodiments, a total number of E or D in X is 12. In some embodiments, a total number of E or D in X is at most 15. In some embodiments, a total number of E or D in X is 15. In some embodiments, a total number of E or D in X is at most 14. In some embodiments, a total number of E or D in X is 14. In some embodiments, a total number of E or D in X is at most 13. In some embodiments, a total number of E or D in X is 13. In some embodiments, a total number of E or D in X is at most 12. In some embodiments, a total number of E or D in X is 12. In some embodiments, a total number of E or D in X is at most 11. In some embodiments, a total number of E or D in X is 11. In some embodiments, a total number of E or D in X is at most 10. In some embodiments, a total number of E or D in X is 10.

[0267] In some embodiments, X of formula (VII) is a moiety comprising 40 to 65 amino acids, and a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30. In some embodiments, X of formula (VII) is a moiety comprising 40 to 65 amino acids, and a total number of R, K, T, A, N, Q, D, E, S, and G in X is 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40. In some embodiments, X of formula (VII) is a moiety comprising 40 to 65 amino acids, and a total number of W, Y, F, M, L, I, and V in X is no more than 20. In some embodiments, X of formula (VII) is a moiety comprising 40 to 65 amino acids, and a total number of W, Y, F, M, L, I, and V in X is 19, 18, 17, 16, 15 or 14.

[0268] In some embodiments, 40-65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at least 40% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at least 45% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at least 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at least 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some

embodiments, at most 65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at most 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at most 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at most 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, at most 45% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0269] In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in Y is no more than 10. In some embodiments, a total number of R, K, T, A, N, Q, D, E, S, and G in Y is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10. In some embodiments, a total number of W, Y, F, M, L, I, and V in Y is no more than 15. In some embodiments, a total number of W, Y, F, M, L, I, and V in Y is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15.

[0270] In some embodiments, X of formula (VII) comprises a sequence having at least 70% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence having at least 75% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence having at least 80% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence having at least 85% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence having at least 90% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence having at least 95% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 96. In some embodiments, X of formula (VII) comprises a sequence of SEQ ID NO: 96. In some embodiments, X of formula (VII) is a sequence of SEQ ID NO: 96.

[0271] In some embodiments, Y of formula (VII) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) comprises a sequence that is any one selected from SEQ ID NOs: 97-103. In some embodiments, Y of formula (VII) is a sequence that is any one selected from SEQ ID NOs: 97-103.

[0272] In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 85% identity

with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) comprises a sequence that is any one selected from SEQ ID NOs: 104-110. In some embodiments, the artificial polypeptide of formula (VII) is a sequence that is any one selected from SEQ ID NOs: 104-110.

[0273] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I),

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0274] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0275] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0276] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0277] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I).

[0278] In some embodiments, at least 20% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 25% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 35% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 40% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 45% amino acids of X in the mutant

are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 55% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 65% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 70% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 75% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 85% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H.

[0279] In some embodiments, X in the mutant comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 75% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 95% identity with SEQ ID NO: 1.

[0280] In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 5. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 5. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 4. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 4. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 3. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 3. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 2. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 2. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 1. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is less than 1. In some embodiments, Y in the mutant can be a moiety comprising 10 to 50 amino acids, and a total number of Cysteine (C) of Y is 0.

[0281] In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 8. In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 9. In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 10. In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 11. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 12. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 13. In some

embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 14. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 15.

[0282] In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 5. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 5. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 4. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 4. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 3. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 3. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 2. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 2. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 1. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 1.

[0283] In some embodiments, Y in the mutant comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence of any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85. In some embodiments, Y in the mutant is a sequence of any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85.

[0284] In some embodiments, Y in the mutant comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85. In some embodiments, Y in the mutant comprises a sequence of any one selected from SEQ ID NOs: 3-18, 58-61

and 84-85. In some embodiments, Y in the mutant is a sequence of any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85.

[0285] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II),

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0286] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0287] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0288] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0289] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II).

[0290] In some embodiments, at least 20% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 25% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 35% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 40% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 45% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 55% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 65% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 70% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 75% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at

most 80% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 85% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H.

[0291] In some embodiments, X in the mutant comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 75% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 95% identity with SEQ ID NO: 1.

[0292] In some embodiments, Y in the mutant comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 55% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 60% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 65% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 75% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 85% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 90% identity with SEQ ID NO: 2.

[0293] In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 8. In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 9. In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 10. In some embodiments, a total number of hydrophobic amino acids in Y in the mutant is more than 11. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 12. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 13. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 14. In some embodiments, the total number of hydrophobic amino acids in Y in the mutant is more than 15.

[0294] In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 5. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 5. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 4. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 4. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 3. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 3. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 2. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 2. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is 1. In some embodiments, a total number of hydrophilic amino acids in Y in the mutant is no more than 1.

[0295] In some embodiments, Y in the mutant comprises a sequence having at least 70% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence having at least 75% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence having at least 85% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant comprises a sequence of any one selected from SEQ ID NOs: 16-18. In some embodiments, Y in the mutant is a sequence of any one selected from SEQ ID NOs: 16-18.

[0296] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III),

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0297] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0298] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0299] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0300] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III).

[0301] In some embodiments, at least 20% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 25% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X in the mutant are selected from

R, K, N, D, Q, E, and H. In some embodiments, at least 35% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 40% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 45% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 55% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 65% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 70% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 75% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 85% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H.

[0302] In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 33. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 32. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 31. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 30. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 29. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 28. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 27. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 26. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 25. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 24. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 23. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 22. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 21. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of H, R, K, D, Q, N and E in X is less than 20.

[0303] In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 10. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 11. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of

hydrophilic amino acids in X is more than 12. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 13. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 14. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 15. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 16. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 17. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 18. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 19. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 20. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 21. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 22. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 23. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 24. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 25.

[0304] In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 14. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 13. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 12. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 11. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 10. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 5.

[0305] In some embodiments, X in the mutant comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 75% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 95% identity with SEQ ID NO: 1.

[0306] In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 70% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 75% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence of SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety that is a sequence of SEQ ID NO: 2.

[0307] In some embodiments, Y in the mutant is hydrophobic moiety, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 70% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 75% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 80% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 85% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 90% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0308] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV),

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0309] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0310] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0311] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0312] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV).

[0313] In some embodiments, at least 20% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 25% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 35% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 40% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 45% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 55% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 65% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 70% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 75% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 85% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H.

[0314] In some embodiments, X in the mutant comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 10. In some embodiments, X in the mutant comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 15. In some embodiments, X in the mutant comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 20. In some embodiments, X in the mutant comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 25. In some embodiments, X in the mutant comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 30. In some embodiments, X in the mutant comprises 40 to 65 amino acids, and a total number of hydrophilic amino acids in X is more than 35.

[0315] In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 15. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 14. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total

number of hydrophobic amino acids in X is no more than 13. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 12. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 11. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 10. In some embodiments, X in the mutant is a moiety comprising 40 to 65 amino acids, and a total number of hydrophobic amino acids in X is no more than 5.

[0316] In some embodiments, X in the mutant comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 75% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 95% identity with SEQ ID NO: 1.

[0317] In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 70% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 75% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 85% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 90% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 95% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence having at least 96%, at least 97%, at least 98%, or at least 99% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety comprising a sequence of SEQ ID NO: 2. In some embodiments, Y in the mutant is a moiety that is a sequence of SEQ ID NO: 2.

[0318] In some embodiments, Y in the mutant is hydrophobic moiety, at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 55% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 60% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 65% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 70% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 75% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 80% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 85% amino acids of Y are selected from I, V, L, F, C, M, and A. In some embodiments, Y in the mutant is hydrophobic moiety, at least 90% amino acids of Y are selected from I, V, L, F, C, M, and A.

[0319] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V),

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

[0320] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0321] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0322] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0323] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V).

[0324] In some embodiments, at least 20% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 25% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 30% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 35% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 40% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 45% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at least 50% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 55% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 60% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 65% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 70% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 75% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 80% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 85% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H. In some embodiments, at most 90% amino acids of X in the mutant are selected from R, K, N, D, Q, E, and H.

[0325] In some embodiments, Y in the mutant comprises 10 to 25 amino acids. In some embodiments, Y in the mutant comprises 10 to 20 amino acids. In some embodiments, Y in the mutant comprises 10 to 15 amino acids. In some embodiments, Y in the mutant comprises 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 amino acids.

[0326] In some embodiments, X in the mutant comprises a sequence having at least 70% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 75% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 80% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 85% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 90% identity with SEQ ID NO: 1. In some embodiments, X in the mutant comprises a sequence having at least 95% identity with SEQ ID NO: 1.

[0327] In some embodiments, Y in the mutant comprises a sequence having at most 50% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 55% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 60% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 65% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 70% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 75% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 80% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 85% identity with SEQ ID NO: 2. In some embodiments, Y in the mutant comprises a sequence having at most 90% identity with SEQ ID NO: 2.

[0328] In another aspect, provided is a method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0329] In another aspect, provided is a method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0330] In another aspect, provided is a method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0331] In another aspect, provided is a method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0332] In another aspect, provided is a method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

[0333] In some embodiments, the polypeptide has at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide has at least 75% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide has at least 80% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide has at least 85% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide has at least 90% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide has at least 95% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide has at least 96%, at least 97%, at least 98%, or at least 99% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide comprises or is an amino acid sequence of any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, or a fragment or variant thereof. In some embodiments, the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74. In some embodiments, the polypeptide is a polypeptide of any one of SEQ ID NOs: 28 and 62-74. In some embodiments, the polypeptide is a polypeptide of SEQ ID NO: 28.

[0334] In another aspect, provided is an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), or a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof, for use in preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, improving nerve conduction velocity in a subject in need thereof, increasing intraepidermal nerve fiber density in a subject in need thereof, or any combination thereof.

[0335] In another aspect, provided is use of an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), or a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof for the preparation of a medicament for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need

thereof, improving nerve conduction velocity in a subject in need thereof, increasing intraepidermal nerve fiber density in a subject in need thereof, or any combination thereof.

[0336] In some embodiments, the medicament is a medicament for use in human.

[0337] In some embodiments, the medicament is a veterinary medicament.

[0338] In some embodiments of either of the above aspects, the subject is a mammal. In some embodiments, the subject is any one selected from the group consisting of a human, primate, rodent, canine, feline, equine, ovine and porcine. In some embodiments, the subject is a human. In some embodiments, the subject is an infant, a toddler, a child, an adolescent, an adult, or an elderly. In some embodiments, the subject is a man or a woman. In some embodiments, the subject is a pet. In some embodiments, the subject is any one selected from the group consisting of mice, rat, guinea pig, gerbil, hamster, chinchilla, rabbit, ferret, cat, dog and pig.

[0339] In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy. In some embodiments, the peripheral neuropathy is mononeuropathy. In some embodiments, the peripheral neuropathy is mononeuritis multiplex. In some embodiments, the peripheral neuropathy is polyneuropathy.

[0340] In some embodiments, the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy. In some embodiments, the peripheral neuropathy is motor neuropathy. In some embodiments, the peripheral neuropathy is sensory neuropathy. In some embodiments, the peripheral neuropathy is autonomic neuropathy.

[0341] In some embodiments, the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency. In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the peripheral neuropathy is associated with compression. In some embodiments, the peripheral neuropathy is associated with traumatic injury. In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the peripheral neuropathy is associated with exposure to toxic chemical agents. In some embodiments, the peripheral neuropathy is associated with radiation therapy. In some embodiments, the peripheral neuropathy is associated with excessive alcohol consumption. In some embodiments, the peripheral neuropathy is associated with vitamin deficiency.

[0342] In some embodiments, the peripheral neuropathy is associated with medical condition. In some embodiments, the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia. In some embodiments, the medical condition is

inflammation. In some embodiments, the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis. In some embodiments, the medical condition is infection. In some embodiments, the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection. In some embodiments, the infection is viral infection. In some embodiments, the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection. In some embodiments, the medical condition is tumor. In some embodiments, the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma. In some embodiments, the medical condition is immune system disease. In some embodiments, the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

[0343] In some embodiments, the peripheral neuropathy is associated with medication. In some embodiments, the medication is treatment with chemotherapeutic agent and/or antibiotic. In some embodiments, the medication is treatment with chemotherapeutic agent. In some embodiments, the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin. In some embodiments, the chemotherapeutic agent is platinum-based antineoplastic drug. In some embodiments, the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate. In some embodiments, the platinum-based antineoplastic drug is cisplatin. In some embodiments, the chemotherapeutic agent is microtubule inhibitor. In some embodiments, the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin. In some embodiments, the microtubule inhibitor is taxoid. In some embodiments, the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel. In some embodiments, the microtubule inhibitor is Vinca alkaloid. In some embodiments, the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine. In some embodiments, the chemotherapeutic agent is Topoisomerase II inhibitor. In some embodiments, the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin. In some embodiments, the chemotherapeutic agent is immunomodulator. In some embodiments, the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide. In some embodiments, the chemotherapeutic agent is proteasome inhibitor. In some embodiments, the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib. In some embodiments, the chemotherapeutic agent is suramin. In some embodiments, the medication is treatment with antibiotic. In some embodiments, the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

[0344] In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN). In some embodiments, the peripheral neuropathy is diabetic peripheral neuropathy. In some embodiments, the peripheral neuropathy is chemotherapy-induced peripheral neuropathy (CIPN), e.g., peripheral neuropathy induced by a platinum-based antineoplastic drug (e.g., cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate).

[0345] In some embodiments, the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction. In some embodiments, the nerve injury associated with peripheral neuropathy is impaired nerve cells. In some embodiments, the nerve injury associated with peripheral neuropathy is impaired nerve fibers. In some embodiments, the nerve injury associated with peripheral neuropathy is impaired nerve conduction.

[0346] In some embodiments, the nerve conduction velocity of a subject is improved after receiving at least one dose of an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI), or (VII), or a mutant of artificial polypeptide of (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity with any one selected from SEQ ID NO. 28, SEQ ID NOs. 57 and 62-74 or a fragment or variant thereof. In some embodiments, the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

[0347] In some embodiments of either of the above aspects, the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy. In some embodiments, the subject is afflicted by peripheral neuropathy. In some embodiments, the subject is in the risk of developing peripheral neuropathy.

[0348] In some embodiments of either of the above aspects, the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to peripheral neuropathy. In some embodiments, the subject does not manifest pain attributable to nerve injury associated with peripheral neuropathy. In some embodiments, the subject does not manifest peripheral neuropathic pain.

[0349] In some embodiments of either of the above aspects, the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy. In some embodiments, the subject manifests one or more symptoms associated with peripheral neuropathy. In some embodiments, the subject is in the risk of developing one or more symptoms associated with peripheral neuropathy. In some embodiments, the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

[0350] In some embodiments of either of the above aspects, the subject does not experience death attributable to administration of at least one dose of the polypeptides of the present disclosure.

[0351] In some embodiments, the subject does not experience poor mental state attributable to administration of at least one dose of the polypeptides of the present disclosure.

[0352] In some embodiments, the subject does not experience altered (e.g., deteriorated) behavioral activity attributable to administration of at least one dose of the polypeptides of the present disclosure.

[0353] In some embodiments, the subject does not experience altered (e.g., deteriorated) eating situation attributable to administration of at least one dose of the polypeptides of the present disclosure.

[0354] In some embodiments, the subject does not experience altered (e.g., deteriorated) fecal property attributable to administration of at least one dose of the polypeptides of the present disclosure.

[0355] In some embodiments, the subject does not experience weight loss attributable to administration of at least one dose of the polypeptides of the present disclosure.

[0356] In some embodiments, the polypeptides of the present disclosure, e.g., an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI) or (VII), or a mutant of an artificial polypeptide of formula (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity (e.g., at least 80% identity) with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof is administered in the form of a formulation comprising the polypeptides of the present disclosure and a pharmaceutically acceptable excipient.

[0357] In some embodiments, the formulation is in a form suitable for oral administration. In some embodiments, the formulation is in a form of a tablet, capsule, pill, powder, granule, solution, suspension or emulsion.

[0358] In some embodiments, the formulation is in a form suitable for parenteral administration. In some embodiments, the formulation is in a form of a sterile solution, suspension, emulsion, gel (e.g., injectable hydrogel) or a sterile powder for injection.

[0359] In some embodiments, the formulation is in a form suitable for topical administration. In some embodiments, the formulation is in a form of a spray, aerosol, powder for inhalation, ointment, cream, patch, suppository, paste, pellicle or gel.

[0360] In some embodiments, the formulation is in a form of sustained, controlled or delayed release formulation. In some embodiments, the formulation is in a form of a matrix tablet, compressed tablet with mixed particles having various rate of release, osmotic pump tablet, sustained or controlled release capsule or microcapsule, sustained or controlled release implant, sustained or controlled release particle, microparticle or microsphere, enteric coated capsule or tablet, colon-located formulation, gel (e.g., hydrogel), liposome, ion-exchange resin, floating formulation, bio-adhesive formulation, stimuli inducing release formulation and pulsatile drug delivery system.

[0361] In some embodiments, the formulation is a formulation for use in human.

[0362] In some embodiments, the formulation is a veterinary formulation.

[0363] More details of these formulations are as described hereinafter in the section entitled "FORMULATION".

FORMULATION

[0364] In another aspect, provided herein is a formulation comprising the polypeptides of the present disclosure, e.g., an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI) or (VII), or a mutant of an artificial polypeptide of formula (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity (e.g., at least 80% identity) with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof and a pharmaceutically acceptable excipient. For the purpose of conciseness, the polypeptides of the present disclosure are sometimes termed as "active ingredients" hereinafter.

[0365] The formulation as described in the present disclosure may be provided in any suitable form, depending on the route of administration. In some embodiments, the formulation is formulated for oral, buccal, topical, transdermal, rectal, intranasal, intrapulmonary, transmucosal, inhalation, or parenteral such as intravenous, intraarterial, intramuscular, subcutaneous, intraosseous or intraperitoneal administration.

[0366] In some embodiments of the formulation, the formulation is in a form suitable for oral administration. In some embodiments, the formulation is in a form of a tablet, capsule, pill, powder, granule, solution, suspension or emulsion. The formulation may comprise a predetermined amount of active ingredients.

[0367] In some embodiments, the formulation is formulated as a tablet. The tablet may comprise a coating that protects it from the acidic environment of the stomach. For example, the coating may be an enteric coating that maintains its integrity in the stomach and releases the active ingredients in the intestine. In some embodiments, the formulation is formulated as a capsule. The capsule can contain a liquid excipient such as a fatty oil. In some embodiments, the formulation is formulated as various liquid oral formulations, such as aqueous solutions, emulsions, or suspensions. In some embodiments, the liquid oral formulations are solutions and/or suspensions reconstituted from non-effervescent granules or effervescent granules. Aqueous solutions include, for example, elixirs and syrups. Elixirs are clear, sweetened, hydroalcoholic preparations. Syrups are concentrated aqueous solutions of a sugar, for example, sucrose, and may contain one or more preservatives. Emulsions are two phase systems in which one liquid is dispersed in the form of small globules throughout another liquid. Emulsions may be oil in water or water in oil emulsions. Excipients used in emulsions are non-aqueous liquids, emulsifying agents and preservatives. Suspensions are heterogeneous mixtures in which the solute particles do not dissolve, but get suspended throughout the bulk of the solvent, left floating around freely in the medium. Suspensions use suspending agents and preservatives. Acceptable substances used in non-effervescent granules, to be reconstituted into a liquid oral formulation, include diluents, sweeteners and wetting agents. Acceptable substances used in effervescent granules, to be reconstituted into a liquid oral formulation, include organic acids and a source of carbon dioxide. Coloring and flavoring agents are used in all of the above formulations.

[0368] In some embodiments of the formulation, the formulation is in a form suitable for parenteral administration. In some embodiments, the formulation is in a form of a sterile solution, suspension, emulsion, gel (e.g., injectable hydrogel) or a sterile powder for injection. The formulation may comprise a predetermined amount of active ingredients.

[0369] In some embodiments, the formulation is formulated as an injection. Examples of injections include, but not limited to a sterile solution, suspension or emulsion in aqueous or oily vehicles. Aqueous

solutions in saline are conventionally used for injections. Ethanol, glycerol, propylene glycol, liquid polyethylene glycol, cyclodextrin derivatives, and vegetable oils may also be used. Oily vehicles that may be used in injections include, but are not limited to lipophilic solvents such as fatty oils or synthetic fatty acid esters. Aqueous injection suspensions may also contain substances such as humectants, suspending agents, and/or flocculating agents or deflocculating agents. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. The formulation may also be formulated for bolus injection or continuous infusion. Alternatively, the formulation may be freeze-dried or in powder form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water, immediately before use (i.e., a sterile powder for injection).

[0370] In some embodiments of the formulation, the formulation is in a form suitable for topical administration. In some embodiments, the formulation is in a form of a spray, aerosol, powder for inhalation, ointment, cream, patch, suppository, paste, pellicle or gel. The formulation may comprise a predetermined amount of active ingredients.

[0371] In some embodiments, the formulation is formulated as a topical formulation, such as for topical application to the skin and mucous membranes. A useful topical formulation for the active ingredients may be a cream, a gel, an ointment, a paste, an aerosol, a spray, a suppository or any other formulations suitable for topical administration. For example, the active ingredients may also be formulated as aerosols for topical application, such as by inhalation. These formulations for administration to the respiratory tract can be in the form of an aerosol for a nebulizer, or as a microfine powder for insufflation, alone or in combination with an inert carrier such as lactose. In such a case, the particles of the formulation will, in some embodiments, have mass median geometric diameters of less than 5 microns, in other embodiments less than 10 microns.

[0372] In some embodiments of the formulation, the formulation is in a form of sustained, controlled or delayed release formulation. In some embodiments, the formulation is in a form of a matrix tablet, compressed tablet with mixed particles having various rate of release, osmotic pump tablet, sustained or controlled release capsule or microcapsule, sustained or controlled release implant, sustained or controlled release particle, microparticle or microsphere, enteric coated capsule or tablet, colon-located formulation, gel (e.g., hydrogel), liposome, ion-exchange resin, floating formulation, bio-adhesive formulation, stimuli inducing release formulation and pulsatile drug delivery system.

[0373] In some embodiments, the formulation is formulated as a sustained release formulation. Examples of sustained release formulations include, but not limited to shaped articles (e.g., sustained release (micro)capsules) formed by semipermeable matrices of solid hydrophobic polymers. Examples of sustained release matrices include, but not limited to hydrogels, polylactides, polyesters, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers, copolymers of L-glutamic acid and γ-ethyl-L-glutamate, and poly-D-(-)-3-hydroxybutyric acid.

[0374] In some embodiments, the formulation is formulated as a controlled release formulation. Such formulations can be used to provide controlled release of one or more active ingredients using, for example,

hydroxypropylmethyl cellulose, other polymer matrices, gels, permeable membranes, osmotic systems, multilayer coatings, microparticles, liposomes, microspheres, or a combination thereof to provide the desired release profile in varying proportions. All controlled release formulations have a common goal of improving drug therapy over that achieved by their non controlled counterparts. Most controlled release formulations are designed to initially release an amount of an active ingredient that promptly produces the desired preventive or therapeutic effect, and gradually and continually release of other amounts of the active ingredient to maintain this level of preventive or therapeutic effect over an extended period of time. In order to maintain this constant level of the active ingredient in the body, the active ingredient must be released from the formulation at a rate that will replace the amount of the active ingredient being metabolized and excreted from the body. Controlled release of an active ingredient can be stimulated by various conditions including, but not limited to, pH, temperature, enzymes, water, or other physiological conditions. Advantages of controlled release formulations include extended activity of the active ingredient, reduced dosage frequency, and increased patient compliance. In addition, controlled release formulations can be used to affect the time of onset of action or other characteristics, such as blood levels of the active ingredient, and can thus affect the occurrence of unwanted side effects. Suitable controlled release formulations can be readily selected for use with the active ingredients provided in the present disclosure.

[0375] In some embodiments, the formulation is a formulation for use in human.

[0376] In some embodiments, the formulation is a veterinary formulation.

[0377] In some embodiments, the formulation is formulated and administered in unit dosage forms or multiple dosage forms. Unit dose forms as used in the present disclosure refer to physically discrete units suitable for a subject in need thereof and packaged individually as is known in the art. Each unit dose contains a predetermined quantity of the active ingredients sufficient to produce the desired preventive or therapeutic effect, in association with one or more pharmaceutically acceptable excipients. Examples of unit dose forms include, but not limited to ampoules and syringes and individually packaged tablets or capsules. Unit dose forms may be administered in fractions or multiples thereof. A multiple dosage form is a plurality of identical unit dosage forms packaged in a single packaging to be administered in segregated unit dose form. Examples of multiple dosage forms include vials, bottles of tablets or capsules, or bottles of pints or gallons. Hence, a multiple dosage form is a multiple of unit doses which are not segregated in packaging.

[0378] The formulations as described in the present disclosure may be prepared using procedures well known in the art (see, e.g., Ansel, Introduction to Pharmaceutical Dosage Forms, Seventh Edition (1999)). The procedures typically include the step of bringing the active ingredients into association with one or more pharmaceutically acceptable excipients. In general, the formulations are prepared by uniformly and intimately admixing the active ingredients with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product into the desired form. For example, a tablet can be prepared by compression or molding the active ingredients, optionally with one or more pharmaceutically acceptable accessory excipients. In instances in which the active ingredients exhibit insufficient solubility, methods

for solubilization may be used such as use of liposomes, prodrugs, complexation/chelation, nanoparticles, or emulsions or tertiary templating.

[0379] Any pharmaceutically acceptable excipients which are conventionally used in the pharmaceutical industry may be employed for the preparation of formulations as described in the present disclosure. The Examples of pharmaceutically acceptable excipients useful for the preparation of the formulations as described in the present disclosure may include, but not limited to: solvents, such as water, ethanol, glycerin, propylene glycol, DMSO, polyethylene glycol, fatty oils such as sesame oil, corn oil, cottonseed oil, or peanut oil, liquid paraffin, ethyl oleate, or isopropyl myristate; surfactants, such as sulfates, sulfonates, quaternary ammoniun compounds, lecithin, Spans, Tweens, Myri, polyoxyl 40 stearate, peregol O, or poloxamers; emulsifying agents, such as gelatin, acacia, tragacanth, bentonite or surfactants such as polyoxyethylene sorbitan monooleate; suspending agents, such as sodium carboxymethylcellulose, pectin, tragacanth, Veegum or acacia; fillers, such as lactose, sucrose, trehalose, lysine, leucine, kaolin, dicalcium phosphate, mannitol, microcrystalline cellulose, or pregelatinized starch; adhesives such as celluloses, PVP, or dextrin; disintegrants, such as croscarmellose sodium, sodium starch glycolate, alginic acid, corn starch, potato starch, bentonite, methylcellulose, agar, or hydroxypropyl starch; lubricants, such as talc, polyethylene glycol, calcium stearate, magnesium stearate, lycopodium or stearic acid; glidants, such as colloidal silicon dioxide; colorants, such as any of the approved certified water soluble FD and C dyes or water insoluble FD and C dyes (e.g., those suspended on alumina hydrate); wetting agents, such as propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate or polyoxyethylene lauryl ether; enteric coating agents, such as fatty acids, fats, waxes, shellac, ammoniated shellac or cellulose acetate phthalates; film coating agents, such as hydroxyethylcellulose, sodium carboxymethylcellulose, polyethylene glycol 4000 or cellulose acetate phthalate; modified release agents, such as polymers such as the Eudragit® series and cellulose esters; sweeteners, such as fructose, glucose, sucrose, artificial sweetening agents such as sucralose, aspartame or saccharin, agave syrup, maple syrup, or corn syrup; flavoring agents, such as natural flavors extracted from plants such as fruits, peppermint, or methyl salicylate; buffers, such as citrate, phosphate, and other organic acids and/or salts thereof; antioxidants, such as ascorbic acid, methionine, citric acid, D,L-α-tocopherol, BHA, BHT, monothioglycerol, ascorbyl palmitate, ascorbic acid, or propyl gallate; preservatives, such as benzoic acid, sodium benzoate, parabens such as methyl paraben or propyl paraben, sorbic acid or benzalkonium bromide; pH modifying agents, such as citric acid, sodium citrate, hydrochloric acid, NaOH or other mild acids or bases; and chelating agents or other materials capable of binding metal ions, such as ethylene diamine tetra acetic acid (EDTA) or its salts.

[0380] The levels of active ingredients in the formulation as described in the present disclosure are effective for delivery of an amount, upon administration that treats, leads to prevention, or amelioration of one or more of the symptoms of diseases or conditions described in the present disclosure. Specifically, the amounts of the active ingredients as described in the present disclosure will be dependent on the subject being treated, the severity of the diseases or conditions, the rate of administration, the absorption, inactivation and excretion rates of the active ingredients being administered, the discretion of the

prescribing physician as well as other factors known to the person skilled in the art. In some embodiments, the formulation comprises from 0.05% to 80%, from 0.1% to 50%, from 0.2% to 40%, from 0.5% to 25%, from 1% to 20%, from 5% to 15%, or from 7% to 12% (wt/wt) of the active ingredients as described in the present disclosure. The balance of the formulation is made up from one or more pharmaceutically acceptable excipients.

[0381] Alternatively, in some embodiments, the formulation comprises from about 0.001 μM to about 100 μM of the active ingredients. In some embodiments, the formulation comprises from about 0.01 μM to about 20 μM of the active ingredients. In some embodiments, the formulation comprises from about 0.1 μM to about 5 μM of the active ingredients. In some embodiments, the formulation comprises from about 0.2 μM to about 3μM of the active ingredients. In some embodiments, the formulation comprises from about 0.1 μM to about 10 μM of the active ingredients. In some embodiments, the formulation comprises from about 1 μM to about 5 μM of the active ingredients. In some embodiments, the formulation comprises from about 1 μM to about 10 μM of the active ingredients. In some embodiments, the formulation comprises from about 5 μM to about 10 μM of the active ingredients. In some embodiments, the formulation comprises from about 10 μM to about 50 μM of the active ingredients. In some embodiments, the formulation comprises from about 20 μM to about 50 μM of the active ingredients. In some embodiments, the formulation comprises from about 5 μM to about 50 μM of the active ingredients. In some embodiments, the formulation comprises from about 1 μM to about 50 μM of the active ingredients. In some embodiments, the formulation comprises from about 1 μM to about 20 μM of the active ingredients. In some embodiments, the formulation comprises from about 5 μM to about 20 μM of the active ingredients. In some embodiments, the formulation comprises from about 10 μM to about 20 μM of the active ingredients. In some embodiments, the formulation comprises higher than about 0.001, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7. 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2,8, 2.9, or 3.0 μM of the active ingredients. In some embodiments, the formulation comprises lower than 100, 90, 80, 70, 60, 50, 40, 30, 20, 25, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, or 4 μM of the active ingredients.

PREPARATION OF THE POLYPEPTIDE

[0382] The polypeptides of the present disclosure, e.g., an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI) or (VII), or a mutant of an artificial polypeptide of formula (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity (e.g., at least 80% identity) with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof can be prepared by any suitable method, including but not limited to molecular cloning techniques and synthetic procedures. Standard molecular cloning techniques are well known in the art and are described by Sambrook, J., Fritsch, E. F. and Maniatis, T. Molecular Cloning: A Laboratory Manual; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, (1989) (Maniatis) and by T. J. Silhavy, M. L. Bennan, and L. W. Enquist, Experiments with Gene Fusions, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y. (1984) and by Ausubel, F. M. et

al., Current Protocols in Molecular Biology, pub. by Greene Publishing Assoc. and Wiley-Interscience (1987).

[0383] In some embodiments, the polypeptides of the present disclosure are prepared by reference to the fermentation-based manufacturing method as disclosed in Chinese patent application No. 201711320516.4 (Publication No.: CN109913483A), which is herein incorporated by reference in its entirety. In some embodiments, the method for preparing the polypeptides of the present disclosure comprises the steps of: integrating a target gene fragment into an expression plasmid by means of genetic engineering, with the integrated target gene fragment comprising at least one purification tag; transforming the expression plasmid into a corresponding expression host to construct a recombinant engineered cell which highly expresses the target polypeptide; subjecting the recombinant engineered cell to fermentation, induced expression, and then crude purification to obtain a crude polypeptide; subjecting the crude polypeptide to refined purification to obtain highly purified polypeptide.

[0384] In some embodiments, the target gene fragment is any one selected from the group consisting of gene fragments which are capable of encoding the polypeptides of the present disclosure, e.g., an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI) or (VII), or a mutant of an artificial polypeptide of formula (I), (II), (III), (IV) or (V), or a polypeptide having at least 70% identity (e.g., at least 80% identity) with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof. In some embodiments, the target gene fragment is a gene fragment which is capable of encoding an artificial polypeptide of formula (I), (II), (III), (IV), (V), (VI) or (VII). In some embodiments, the target gene fragment is a gene fragment which is capable of encoding a mutant of an artificial polypeptide of formula (I), (II), (III), (IV) or (V). In some embodiments, the target gene fragment is a gene fragment which is capable of encoding a polypeptide having at least 70% identity (e.g., at least 80% identity) with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof. The target gene fragment can be prepared by any suitable method, including but not limited to enzymatic synthesis, i.e., using RNA as a template to synthesize cDNA by reverse transcription, and chemical synthesis method, i.e., using a chemical method or chemical method combined with enzymatic method to synthesize target gene. The preparation of target gene fragment may also be commercially conducted by a contract research organization (CRO) in case that the sequence of target gene fragment is provided.

[0385] In some embodiments, the purification tag is a ST sequence tag (an amino acid sequence that helps the polypeptides of the present disclosure to form inclusion bodies) or a His tag.

[0386] In some embodiments, the expression host is a host cell. The host cell includes but is not limited to an individual cell, cell culture, or cell line. In some embodiments, the host cells include progeny of a single host cell. In some embodiments, a host cell can be transfected with a heterologous sequence including vectors encoding the polypeptides of the present disclosure. In some embodiments, said host cells may be prokaryotic cells, such as bacterial cells. In some embodiments, said host cells may be eukaryotic cells, such as yeast cells, animal cells, insect cells, plant cells and the like.

[0387] Examples of bacterial host cells that can be used to produce the polypeptide or the mutant of the present disclosure include microorganisms belonging to the genus *Escherichia, Serratia, Bacillus,*

Brevibacterium, Corynebacterium, Microbacterium, Pseudomonas and the like. For example, bacterial host cells may include, but not be limited to, *Escherichia coli XL1-Blue, XL2-Blue, DH1, MC1000, KY3276, W1485, JM109, HB101, No. 49, i W3110, NY49, G1698, BL21, or TB1.* Other bacterial host cells may include, but not be limited to, *Serratia ficaria, Serratia fonticola, Serratia liquefaciens, Serratia marcescens, Bacillus subtilis, Bacillus amyloliquefaciens, Brevibacterium ammoniagenes, Brevibacterium immariophilum ATCC 14068, Brevibacterium saccharolyticum ATCC 14066, Brevibacterium flavum ATCC 14067, Brevibacterium lactofermentum ATCC 13869, Corynebacterium glutamicum ATCC 13032, Corynebacterium glutamicum ATCC 13869, Corynebacterium acetoacidophilum ATCC 13870, Microbacterium ammoniaphilum ATCC 15354, Pseudomonas putida, Pseudomonas sp. D-0110* and the like.

[0388] Examples of yeast cells that can be used to produce the polypeptides of the present disclosure include microorganisms belonging to the genus *Kluyveromyces, Trichosporon, Saccharomyces, Schizosaccharomyces, Schwanniomyces, Pichia, Candida* and the like, such as *Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces lactis, Trichosporon pullulans, Schwanniomyces alluvius, Candida utilis* and the like.

[0389] Examples of animal cells that can be used to produce the polypeptides of the present disclosure include mammalian cells, for example, Chinese hamster ovary cells (CHO) or monkey cells, such as COS cells, HepG2 cells, A549 cells, and any other cells available through ATCC or other depositories.

[0390] In some embodiments, the expression host is an *Escherichia Coli* host cell. In some embodiments, the formula of the fermentation medium used in the fermentation process is: yeast extract powder 10-50g/L, peptone 10-30g/L, ammonium sulfate 2-10g/L, sodium chloride 2-10g/L, potassium dihydrogen phosphate 0-10g/L, dipotassium hydrogen phosphate 2-15g/L, defoamer 0.01-0.1% (v/v), $FeSO_4 \cdot 7H_2O$ 0-0.1g/L, $ZnSO_4 \cdot 7H_2O$ 0-0.02g/L, $CuSO_4 \cdot 5H_2O$ 0-0.1g/L, $MnSO_4 \cdot 5H_2O$ 0-0.05g/L, $CaCl_2 \cdot 7H_2O$ 0-0.01g/L, $CoCl_2 \cdot 6H_2O$ 0-0.01g/L, $Na_2MoO_4 \cdot 2H_2O$ 0-0.01g/L, H_3BO_3 0-0.0005g/L, and Biotin 0-0.005g/L. In some embodiments, the fermentation process is performed at 37°C.

[0391] In some embodiments, the induced expression is realized by addition of isopropyl-beta-D-thiogalactopyranoside (IPTG) during the fermentation process. In some embodiments, the IPTG is added 0.5, 1, 2, 3, 4 or 5 hours after the initiation of the fermentation process. In some embodiments, the IPTG is added at a final concentration of 0.25, 0.5, 1, 2 or 4 mM. In some embodiments, the induced expression is performed at 37°C.

[0392] The crude purification of the present disclosure is a process during which the culture produced by the fermentation process is preliminary treated. In some embodiments, the crude purification comprises the steps of collecting the cells and isolating the inclusion body proteins and/or cytoplasmic proteins after lysing the cells; subjecting the inclusion body proteins and/or cytoplasmic proteins to denaturation, renaturation and enzymatic digestion to obtain a crude product containing the crude polypeptide. In some embodiments, the crude purification comprises the steps of collecting the culture medium, removing the cells and impurities, and obtaining the supernatant, i.e., a crude product containing the crude polypeptide.

[0393] The refined purification of the present disclosure is a process during which the crude product containing the crude polypeptide is purified with a chromatographic method. Examples of chromatographic methods that can be used to purify the polypeptides of the present disclosure include ion exchange chromatography with a strong anion exchange resin, a weak anion exchange resin or a multimodal anion exchange resin; affinity chromatography; reversed phase chromatography with reversed phase packing materials; molecular sieve chromatography with size exclusion packing materials; and hydrophobic chromatography with hydrophobic packing materials.

[0394] More detailed information for preparing the polypeptides of the present disclosure may be found throughout of the disclosure of CN109913483A, e.g., Examples 1-4.

KIT

[0395] The present disclosure also provides a kit for use in preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, improving nerve conduction velocity in a subject in need thereof, increasing intraepidermal nerve fiber density in a subject in need thereof, or any combination thereof. In some embodiments, the kit comprises one or more of the polypeptides of the present disclosure, and an instruction for using the kit. In some embodiments, the kit comprises one or more formulations described herein, and an instruction for using the kit.

[0396] The kits can comprise one or more containers that contain one or more of the polypeptides of the present disclosure or a formulation comprising the same. The polypeptides of the present disclosure can be present in the container as a prepared formulation, or alternatively, the polypeptides of the present disclosure can be unformulated. In some embodiments, the kit can include the unformulated polypeptides of the present disclosure in a container that is separate from the pharmaceutically acceptable excipients. Prior to use, the polypeptides of the present disclosure is diluted or otherwise mixed with the pharmaceutically acceptable excipients.

[0397] In some embodiments, the kit provided herein also comprises instructions which describe the method for administering the formulations. In some embodiments, the instructions also describe the procedure for mixing the polypeptides of the present disclosure contained in the kit with pharmaceutically acceptable excipients.

[0398] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. It is not intended that the invention be limited by the specific examples provided within the specification. While the invention has been described with reference to the aforementioned specification, the descriptions and illustrations of the embodiments herein are not meant to be construed in a limiting sense. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. Furthermore, it shall be understood that all aspects of the invention are not limited to the specific

depictions, configurations or relative proportions set forth herein which depend upon a variety of conditions and variables. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is therefore contemplated that the invention shall also cover any such alternatives, modifications, variations or equivalents. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

EXAMPLES

[0399] The present disclosure will now be described with reference to the following Example, which is intended to illustrate, but not limit, the invention.

[0400] Unless otherwise specified, if the specific conditions are not indicated in the Example, it is carried out in accordance with the conventional conditions or the conditions suggested by the manufacturer. The reagents or instruments used without the manufacturer's indication are conventional products that commercially available. Those skilled in the art would understand that the Example described herein is not intended to limit the scope of the invention as claimed.

Example 1: Neuroprotective effect of the polypeptide of the present disclosure administered via intravenous injection route on a diabetic peripheral neuropathy (DPN) model of cynomolgus monkeys induced by high-sugar and high-fat diet

[0401] In this Example, the neuroprotective effect of an exemplary polypeptide of the present disclosure, i.e. SEQ ID NO: 29 administered via intravenous injection (i.v.) route was investigated in a diabetic peripheral neuropathy (DPN) model of cynomolgus monkeys induced by high-sugar and high-fat diet.

[0402] *Screening and enrollment of experimental animals*

[0403] 13 animals aging 18 to 20 years old and weighting 7 to 13 kg were screened among a group of male non-naive cynomolgus monkeys (provided by Hainan Jingang Biotech., Co., Ltd. and Suzhou Xishan Zhongke Pharmaceutical Research and Development Co., Ltd.) who were fed a high-fat feed accompanied by 20% high-fructose drinking water or fed a mixture of high-fat feed and high-fructose feed for more than 4 years, of which 7 animals were hyperglycemic (blood test GLU > 8.0 mmol/L in the past and before the start of the experiment), and 6 animals did not have obvious hyperglycemia (2.0 mmol/L < blood test GLU < 6.0 mmol/L in the past and before the start of the experiment). The animals were subjected to nerve conduction tests (including conduction tests for median motor and sensory nerves, tibial nerve, common peroneal nerve (motor) and superficial peroneal nerve (sensory)) and thermal pain tests. First, based on the past biochemical historical data, one hyperglycemic animal with abnormal historical biochemical indicators was ruled out. 6 hyperglycemic animals displaying abnormal nerve conduction velocity (i.e., the conduction velocity was less than the lower limit of the normal reference value measured during the same time period) (animals held in the same feeding facility environment and condition and with no obviously abnormal heat pain sensation and blood sugar should be checked thoroughly, and the lower limit of the normal reference value denotes the first quartile of the resulting nerve conduction velocities) and sensitivity

to heat pain (escape rate at 44°C exceeded 20% in the test) were screened. And 6 normoglycemic animals with no more than two abnormal nerve conduction velocity indicators and insensitivity to heat pain were screened. Based on the results of animal food intake before administration, 2 animals without obvious hyperglycemia were ruled out.

[0404] *Grouping and administration*

[0405] 10 male cynomolgus monkeys that met the experimental requirements were enrolled in this experiment, of which 4 hypoglycemic animals were allocated to Group 1 (Normal), and 6 hyperglycemic animals were allocated to Group 2 (Diabetes).

[0406] The dosing regimen is shown in Table 1.

[0407] Table 1

Group	N	Model	Test Article	Route	Frequency
Group 1 (Normal)	4	Normal	Normal saline	Intravenous infusion, 30 min, 2 mL/kg, 30 days	1/day
Group 2 (Diabetes)	6	DPN	SEQ ID No: 29	Intravenous infusion, 30 min, 1 mpk, 2 mL/kg, 30 days	1/day

[0408] *Nerve conduction test*

[0409] The conduction velocities of the median nerves and tibial nerves of all animals were detected during the acclimation period (Day -13, Day -8), Day 15, and Day 30. The site of the electrode for recording the motor conduction velocities of the median and tibial nerves was at the muscles controlled by the nerves. The stimulation site was at the proximal end of the nerves. Super strong stimulation was selected as the stimulation intensity (that is, the current intensity when the amplitude of action potential no longer increased as the stimulation current increased × 120%). The sensory conduction velocities of median nerves were measured by the reverse method (i.e., stimulating at the proximal end of the nerves and recording at the distal end of the nerves), and the stimulation intensity was set to the current intensity which evoked a measurable sensory conduction action potential.

[0410] *Results*

[0411] As shown in Fig. 1 and 2, the motor conduction velocities of median nerves in both groups of animals decreased, but the *magnitude* of decrease of the Diabetes group was lower than that of the Normal group. As shown in Fig. 2, compared with the respective values of motor conduction velocities before administration (mean values of Pre1 & Pre2), the Diabetes group displayed a decrease of 5.54 ± 3.06% on Day 30, whereas the Normal group displayed a decrease of 22.38 ± 10.72% on Day 30.

[0412] As shown in Fig. 3 and 4, the sensory conduction velocities of the median nerves of animals in the Normal group decreased on Day 30, whereas the sensory conduction velocities of the median nerves of

animals in the Diabetes group increased on Day 30. These results indicate that the test substance (SEQ ID No: 29) has a certain neuroprotective effect on diabetic peripheral neuropathy.

[0413] As shown in Fig. 5, the motor conduction velocities of the tibial nerves of both groups of animals showed a downward trend, but after 30 days of administration, the animals from the Normal group showed a greater *magnitude* of decrease than that of the animals from the Diabetes group, i.e., 17.27 ± 14.22 % vs 4.34 ± 3.48%, respectively.

Example 2: Neuroprotective effect of the polypeptide of the present disclosure administered via intraperitoneal injection route on a chemotherapy-induced peripheral neuropathy (CIPN) model of mice induced by cisplatin

[0414] In this example, the neuroprotective effect of an exemplary polypeptide of the present disclosure, i.e. SEQ ID NO: 29 administered via intraperitoneal injection (i.p.) route was investigated in a chemotherapy-induced peripheral neuropathy (CIPN) model of mice induced by cisplatin.

[0415] *Grouping and administration*

[0416] Male C57BL/6 mice weighing 22-24 g were selected. At the beginning of the experiment, 56 animals were randomly selected according to the weights of the animals and allocated to Naive group, Vehicle group, SEQ ID NO: 29 15 mg/kg group, SEQ ID NO: 29 30 mg/kg group and SEQ ID NO: 29 60 mg/kg group, respectively. There were 8 animals in the Naive group and 12 animals in each of the other groups.

[0417] From Day 1 to Day 22, the mice were administered according to their groups (normal saline/solution of SEQ ID NO: 29 were administered). The animals from the model groups (all groups except for the Naive group) were all administered intraperitoneally, once a day. From Day 1 to Day 5, and from Day 11 to Day 15, the animals from the model groups were intraperitoneally injected with 2.3 mg/kg cisplatin 2 hours post administration of test articles, once a day, to establish the chemotherapy-induced peripheral neuropathy model.

[0418] The dosing regimen is shown in Table 2.

[0419] Table 2

No.	Model	Group	Dose (mg/kg)	Route (10 mL/kg)	Frequency	N	Test
1	-	Naive	NA	NA	NA	8	The nerve conduction velocity tests were performed 2 hours post administration on Day 21; the
2	CIPN	Vehicle (normal saline)	NA	i.p.	QD*22 days (Once a day, intraperitoneally injected with 2.3 mg/kg cisplatin 2 hours post intraperitoneal injection of normal saline in the morning;	12	

					cisplatin was administered from Day 1 to Day 5, Day 11 to Day 15)		epidermises of the right footpads were collected for immunofluorescence staining 2 hours post administration on Day 22, and the intraepidermal nerve fiber densities (IENFD) were calculated.
3	CIPN	SEQ ID NO: 29	15	i.p.	QD*22 days (Once a day, intraperitoneally injected with 2.3 mg/kg cisplatin 2 hours post intraperitoneal injection of SEQ ID NO: 29 in the morning; cisplatin was administered from Day 1 to Day 5, Day 11 to Day 15)	12	
4	CIPN	SEQ ID NO: 29	30	i.p.	QD*22 days (Once a day, intraperitoneally injected with 2.3 mg/kg cisplatin 2 hours post intraperitoneal injection of SEQ ID NO: 29 in the morning; cisplatin was administered from Day 1 to Day 5, Day 11 to Day 15)	12	
5	CIPN	SEQ ID NO: 29	60	i.p.	QD*22 days (Once a day, intraperitoneally injected with 2.3 mg/kg cisplatin 2 hours post intraperitoneal injection of SEQ ID NO: 29 in the morning; cisplatin was administered from Day 1 to Day 5, Day 11 to Day 15)	12	

Note: NA denotes "not applicable".

[0420] *Nerve conduction velocity test*

[0421] 2 hours post administration on Day 21, 8 animals from each of the Naive group, Vehicle group, and SEQ ID NO: 29 60 mg/kg group (a total of 24 animals) were subjected to nerve conduction velocity tests.

[0422] On the day of the experiment, the animals were deeply anesthetized by intraperitoneal injection of 20 mg/kg Zoletil 50 combined with 8 mg/kg Xylazine hydrochloride solution, and then a recording electrode was embedded at the root of tails and a stimulation electrode was embedded 40 mm from the end of tails, with a stimulation delay of 5 ms and a wave width of 0.1 ms. Stimulation voltage intensities were given sequentially from low to high (starting at 1V) until a sensory nerve action potential (SNAP) was induced with a maximum amplitude of about 120%, and then simulations were performed for 5 times at this intensity, averaged, so the action potential latencies can be read.

[0423] Sensory nerve conduction velocity (m/s) = conduction distance/action potential latency.

[0424] *Histopathological observation*

[0425] Right plantar skin collection: 2 hours post administration on Day 22, the right plantar skins of 8 animals from each of the Naive group, Vehicle group, and SEQ ID NO: 29 60 mg/kg group (a total of 24 animals) were collected and were subjected to immunofluorescence staining and calculation of IENFD values.

[0426] Tissue fixation and dehydration: the footpad skins were fixed in a 4% paraformaldehyde fixative for 24 hours. After fixation, the fixative was replaced with 30% sucrose for dehydration at 4°C.

[0427] Tissue embedding: after tissue dehydration was completed, OCT was used for tissue embedding.

[0428] Frozen sectioning and staining: OCT-embedded tissue blocks were sectioned into 20-micron-thick sections, and the sections were subjected to immunofluorescence staining. The primary antibody was anti-PGP9.5 antibody, and the secondary antibody was Goat Anti-Rabbit IgG H&L (Alexa Fluor 594).

[0429] Image acquisition and analysis of sections: a ZEISS fluorescence microscope was used to capture and acquire images, and a 20X magnification lens was used to acquire images of the protuberant areas of the footpads. The densities of nerve fibers within the epidermises of the footpads were quantitatively analyzed using blind evaluation.

[0430] Histopathological evaluation criteria: with regard to fluorescent staining, a ZEN 3.4 software was used to measure the lengths of the epidermises of the footpads, the numbers of subepidermal nerve fibers of the footpads were manually counted to calculate the intraepidermal nerve fiber densities (nerve fiber density = number of nerve fibers/epidermal length).

[0431] *Results*

[0432] As shown in Fig. 6, the animals from the SEQ ID NO: 29 60 mg/kg group showed significantly increased tail sensory nerve conduction velocities (SNCV) compared with those from the Vehicle group, with p values <0.01 and <0.05, respectively. These results indicate that SEQ ID NO: 29 can significantly prevent the decrease in the conduction velocities of the tail sensory nerves of mice and has a certain neuroprotective effect.

[0433] As shown in Fig. 7, the mice from the Vehicle group showed decrease in the intraepidermal nerve fibers on the right footpad compared with those from the Naive group, whereas the mice from the SEQ ID NO: 29 60 mg/kg group showed increase in the intraepidermal nerve fibers on the right footpad compared with those from the Vehicle group. Furthermore, as shown in Fig. 8, the mice from the SEQ ID NO: 29 60 mg/kg group showed significantly increased intraepidermal nerve fiber densities (IEFND) compared with those from the Vehicle group, with p values <0.01 and <0.05, respectively. These results indicate that SEQ ID NO: 29 can significantly prevent the decrease in intraepidermal nerve fiber densities (IEFND) of the footpads of mice and has a certain neuroprotective effect.

SEQUENCE LISTING

SEQ ID NO	Sequences
1	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA
2	TVLLMILVCETPYGCYVLHQKGRMCSAFLCC
3	TVLLMILVAETPYGAYVLHQKGRMASAFLAA
4	TVLLMILVCETPYGCYVLHQKGRMCSAFLCA
5	TVLLMILVVETPYGVYVLHQKGRMVSAFLVV
6	TVLLMILVAETPYGAYVLHQKGRMVSAFLVV
7	TVLLMILVAETPYGVYVLHQKGRMASAFLVV
8	TVLLMILVAETPYGVYVLHQKGRMVSAFLAV
9	VLLMILVAETPYGVYVLHQKGRMVSAFLVA
10	TVLLMILVVETPYGAYVLHQKGRMASAFLVV
11	TVLLMILVVETPYGAYVLHQKGRMVSAFLAV
12	TVLLMILVVETPYGAYVLHQKGRMVSAFLVA
13	TVLLMILVVETPYGVYVLHQKGRMASAFLAV
14	TVLLMILVVETPYGVYVLHQKGRMASAFLVA
15	TVLLMILVVETPYGVYVLHQKGRMVSAFLAA
16	TVLLVILVAETPYGAYVLHQKGRVASAFLAA
17	GLCALCLMVRQPCFCLEIYMGVKHTCLYVST
18	SLLCVFPTIECCRYKMGLLYHCVACTQGMLV
19	SEFEDANKEQGEVPNDDVSDELPKLLDDDEDELRGALFFQWHDWEEAEDNDWDVEDA
20	SELDFWDNWKDRQADLPAASDDEDFENDLAEVDHEDPLVDGNEWDGDEVEFELEEQK
21	SDADEFDDDNSVWGWEDDEVEPNDAFQPLGDVRANEELDEKDHKLDEEADLQWEFEL
22	SQWAPLDHLESDEWGAFEDEDFNNGDVEELDPEERDDEDLFQKDVLVAKADDEEWDN
23	STKKQPVDLGLLETDSEFTEFPATSWAGLSESESAHVWTSNWDSSNVTSDFSNQLRA
24	STKKQPVDLGLLETDDEFEEFPATSWAGLSEDESAHVWESNWDDSNVTSDFSNQLRA
25	STKKQPVDLGLLEEDDEFEEFPAESWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRA
26	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRA
27	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA
28	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
29	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVAETPYGAYVLHQKGRMASAFLAA
30	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVCETPYGCYVLHQKGRMCSAFLCA
31	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGVYVLHQKGRMVSAFLVV
32	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVAETPYGAYVLHQKGRMVSAFLVV
33	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVAETPYGVYVLHQKGRMASAFLVV
34	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVAETPYGVYVLHQKGRMVSAFLAV
35	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVAETPYGVYVLHQKGRMVSAFLVA
36	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGAYVLHQKGRMASAFLVV
37	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGAYVLHQKGRMVSAFLAV
38	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGAYVLHQKGRMVSAFLVA

39	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGVYVLHQKGRMASAFLAV
40	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGVYVLHQKGRMASAFLVA
41	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVVETPYGVYVLHQKGRMVSAFLAA
42	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAG LCALCLMVRQPCFCLEIYMGVKHTCLYVST
43	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAS LLCVFPTIECCRYKMGLLYHCVACTQGMLV
44	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLVILVAETPYGAYVLHQKGRVASAFLAA
45	SEFEDANKEQGEVPNDDVSDELPKLLDDDEDELRGALFFQWHDWEEAEDNDWDVEDAT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
46	SELDFWDNWKDRQADLPAASDDEDFENDLAEVDHEDPLVDGNEWDGDEVEFELEEQKT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
47	SDADEFDDDNSVWGWEDDEVEPNDAFQPLGDVRANEELDEKDHKLDEEADLQWEFELT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
48	SQWAPLDHLESDEWGAFEDEDFNNGDVEELDPEERDDEDLFQKDVLVAKADDEEWDNT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
49	STKKQPVDLGLLETDSEFTEFPATSWAGLSESESAHVWTSNWDSSNVTSDFSNQLRATVL LMILVCETPYGCYVLHQKGRMCSAFLCC
50	STKKQPVDLGLLETDDEFEEFPATSWAGLSEDESAHVWESNWDDSNVTSDFSNQLRATVL LMILVCETPYGCYVLHQKGRMCSAFLCC
51	STKKQPVDLGLLEEDDEFEEFPAESWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRATV LLMILVCETPYGCYVLHQKGRMCSAFLCC
52	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRAT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
53	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRAT VLLMILVCETPYGCYVLHQKGRMCSAFLCC
54	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRAT VLLMILVCETPYGCYVLHQKGRMCS
55	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRAT VLLMILVCETPYGCYVLHQK
56	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRAT VLLMILVCET
57	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRAT VLLMI
58	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA
59	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA
60	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA
61	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA
62	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAE LEKHGYKMETS
63	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMILVCETPYGCYVLHQKGRMCSAFLCC
64	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMILVCETPYGCYVLHQKGRMCSAFLCC
65	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRV TVLLMILVCETLYGCYVLHQKGRMCSAFLCC
66	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TILLMILVCETPYGCYVLHQKGRMCSAFLCC
67	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMVLVCETPYGCYVLHQKERMCSAFLCC

68	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMIKVYETPYGCYILHQKGRMCSAFLCC
69	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMIKVYETPYGCYILHQKGRMCSAFLCC
70	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMIKVYETPYGCYILHQKGRMCSAFLCC
71	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMKKVYETPYGCYILHQKGRMCSAFLCC
72	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMIKVYETPYGCYILHQKGRMCSAFLCC
73	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMIKVYETPYGCYILHQKGRMCSAFLCC
74	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRA TVLLMIKVYETPYGCYILHQKGRMCSAFLCC
75	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAT VLLMILVAETPYGAYV
76	SEFEDANKEQGEVPNDDVSDELPKLLDDDEDELRGALFFQWHDWEEAEDNDWDVEDA
77	SELDFWDNWKDRQADLPAASDDEDFENDLAEVDHEDPLVDGNEWDGDEVEFELEEQK
78	SDADEFDDDNSVWGWEDDEVEPNDAFQPLGDVRANEELDEKDHKLDEEADLQWEFEL
79	SQWAPLDHLESDEWGAFEDEDFNNGDVEELDPEERDDEDLFQKDVLVAKADDEEWDN
80	STKKQPVDLGLLETDSEFTEFPATSWAGLSESESAHVWTSNWDSSNVTSDFSNQLRA
81	STKKQPVDLGLLETDDEFEEFPATSWAGLSEDESAHVWESNWDDSNVTSDFSNQLRA
82	STKKQPVDLGLLEEDDEFEEFPAESWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRA
83	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRA
84	GLAALALMVRQPAFALEIYMGVKHTALYVST
85	SLLAVFPTIEAARYKMGLLYHAVAATQGMLV
86	SEFEDANKEQGEVPNDDVSDELPKLLDDDEDELRGALFFQWHDWEEAEDNDWDVEDAT VLLMILVAETPYGAYVLHQKGRMASAFLAA
87	SELDFWDNWKDRQADLPAASDDEDFENDLAEVDHEDPLVDGNEWDGDEVEFELEEQKT VLLMILVAETPYGAYVLHQKGRMASAFLAA
88	SDADEFDDDNSVWGWEDDEVEPNDAFQPLGDVRANEELDEKDHKLDEEADLQWEFELT VLLMILVAETPYGAYVLHQKGRMASAFLAA
89	SQWAPLDHLESDEWGAFEDEDFNNGDVEELDPEERDDEDLFQKDVLVAKADDEEWDNT VLLMILVAETPYGAYVLHQKGRMASAFLAA
90	STKKQPVDLGLLETDSEFTEFPATSWAGLSESESAHVWTSNWDSSNVTSDFSNQLRATVL LMILVAETPYGAYVLHQKGRMASAFLAA
91	STKKQPVDLGLLETDDEFEEFPATSWAGLSEDESAHVWESNWDDSNVTSDFSNQLRATVL LMILVAETPYGAYVLHQKGRMASAFLAA
92	STKKQPVDLGLLEEDDEFEEFPAESWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRATV LLMILVAETPYGAYVLHQKGRMASAFLAA
93	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDESAHVWEDNWDDDNVTSDFSNQLRAT VLLMILVAETPYGAYVLHQKGRMASAFLAA
94	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAG LAALALMVRQPAFALEIYMGVKHTALYVST
95	SEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVEDDFSNQLRAS LLAVFPTIEAARYKMGLLYHAVAATQGMLV
96	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA
97	TVLLMILVCETPYGCYVLHQKGRMC
98	TVLLMILVCETPYGCYVLHQKGRM
99	TVLLMILVCETPYGCYVLHQKGR
100	TVLLMILVCETPYGCYVLHQKG
101	TVLLMILVCETPYGCYVLH
102	TVLLMILVCETPYGCYVL
103	TVLLMILVCETPYGCY

104	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCYVLHQKGRMC
105	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCYVLHQKGRM
106	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCYVLHQKGR
107	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCYVLHQKG
108	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCYVLH
109	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCYVL
110	MSEKKQPVDLGLLEEDDEFEEFPAEDWAGLDEDEDAHVWEDNWDDDNVTSDFSNQLRA TVLLMILVCETPYGCY

CLAIMS

WHAT IS CLAIMED IS:

1. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

2. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

3. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

4. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

5. The method of claim 4, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

6. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a total number of Cysteine (C) of less than 5.

7. The method of any one of claims 1 to 6, wherein X comprises a sequence having at least 90% identity with SEQ ID NO: 1, X comprises a sequence having at least 95% identity with SEQ ID NO: 1, or X comprises a sequence of SEQ ID NO: 1.

8. The method of any one of claims 1 to 7, wherein at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H.

9. The method of any one of claims 1 to 8, wherein Y comprises a total number of Cysteine (C) of less than 4, Y comprises a total number of Cysteine (C) of less than 3, or Y comprises a total number of Cysteine (C) of less than 2.

10. The method of any one of claims 1 to 9, wherein a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5.

11. The method of any one of claims 1 to 10, wherein X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 81-83.

12. The method of any one of claims 1 to 11, wherein Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85, or Y comprises a sequence having at least 90% identity with anyone selected from SEQ ID NOs: 3-18, 58-61 and 84-85.

13. The method of any one of claims 1 to 12, wherein the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 29-41, 54-57, 75 and 91-95.

14. The method of claim 1, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

15. The method of claim 1, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

16. The method of claim 1, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

17. The method of claim 1, wherein the peripheral neuropathy is associated with medical condition.

18. The method of claim 17, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

19. The method of claim 18, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

20. The method of claim 18, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

21. The method of claim 20, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

22. The method of claim 18, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

23. The method of claim 18, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

24. The method of claim 1, wherein the peripheral neuropathy is associated with medication.

25. The method of claim 24, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

26. The method of claim 25, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

27. The method of claim 26, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

28. The method of claim 26, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

29. The method of claim 28, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

30. The method of claim 28, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

31. The method of claim 26, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

32. The method of claim 26, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

33. The method of claim 26, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

34. The method of claim 25, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

35. The method of claim 1, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

36. The method of claim 1, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

37. The method of any one of claims 1 to 13, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

38. The method of any one of claims 1 to 13, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

39. The method of any one of claims 1 to 13, wherein the subject does not manifest peripheral neuropathic pain.

40. The method of any one of claims 1 to 13, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

41. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

42. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

43. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

44. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

45. The method of claim 44, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

46. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A;

wherein Y comprises a sequence having at most 90% identity with SEQ ID NO: 2.

47. The method of any one of claims 41 to 46, wherein X comprises a sequence having at least 90% identity with SEQ ID NO: 1, X comprises a sequence having at least 95% identity with SEQ ID NO: 1, or X comprises a sequence of SEQ ID NO: 1.

48. The method of any one of claims 41 to 47, wherein at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H.

49. The method of any one of claims 41 to 48, wherein Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 50% identity with SEQ ID NO: 2.

50. The method of any one of claims 41 to 49, wherein a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5.

51. The method of any one of claims 41 to 50, wherein Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18, or Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18.

52. The method of any one of claims 41 to 51, wherein the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 42-44.

53. The method of claim 41, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

54. The method of claim 41, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

55. The method of claim 41, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

56. The method of claim 41, wherein the peripheral neuropathy is associated with medical condition.

57. The method of claim 56, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

58. The method of claim 57, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

59. The method of claim 57, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

60. The method of claim 59, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

61. The method of claim 57, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

62. The method of claim 57, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

63. The method of claim 41, wherein the peripheral neuropathy is associated with medication.

64. The method of claim 63, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

65. The method of claim 64, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

66. The method of claim 65, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

67. The method of claim 65, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

68. The method of claim 67, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

69. The method of claim 67, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

70. The method of claim 65, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

71. The method of claim 65, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

72. The method of claim 65, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

73. The method of claim 64, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

74. The method of claim 41, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

75. The method of claim 41, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

76. The method of any one of claims 41 to 52, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

77. The method of any one of claims 41 to 52, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

78. The method of any one of claims 41 to 52, wherein the subject does not manifest peripheral neuropathic pain.

79. The method of any one of claims 41 to 52, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

80. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

81. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

82. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

83. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

84. The method of claim 83, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

85. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein a total number of H, R, K, D, Q, N and E in X is less than 33.

86. The method of any one of claims 80 to 85, wherein Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, Y comprises a sequence having at least 95% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2.

87. The method of any one of claims 80 to 86, wherein at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

88. The method of any one of claims 80 to 87, wherein the total number of H, R, K, D, Q, N and E in X is less than 30, the total number of H, R, K, D, Q, N and E in X is less than 25, or the total number of H, R, K, D, Q, N and E in X is less than 20.

89. The method of any one of claims 80 to 88, wherein a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10.

90. The method of any one of claims 80 to 89, wherein X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 23-27, or X comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 23-27.

91. The method of any one of claims 80 to 90, wherein the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 49-53.

92. The method of claim 80, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

93. The method of claim 80, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

94. The method of claim 80, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

95. The method of claim 80, wherein the peripheral neuropathy is associated with medical condition.

96. The method of claim 95, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

97. The method of claim 96, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

98. The method of claim 96, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

99. The method of claim 98, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

100. The method of claim 96, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

101. The method of claim 96, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

102. The method of claim 80, wherein the peripheral neuropathy is associated with medication.

103. The method of claim 102, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

104. The method of claim 103, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

105. The method of claim 104, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

106. The method of claim 104, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

107. The method of claim 106, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

108. The method of claim 106, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

109. The method of claim 104, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

110. The method of claim 104, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

111. The method of claim 104, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

112. The method of claim 103, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

113. The method of claim 80, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

114. The method of claim 80, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

115. The method of any one of claims 80 to 91, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

116. The method of any one of claims 80 to 91, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

117. The method of any one of claims 80 to 91, wherein the subject does not manifest peripheral neuropathic pain.

118. The method of any one of claims 80 to 91, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

119. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

120. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

121. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

122. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

123. The method of claim 122, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

124. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E; and

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

wherein X comprises a sequence having at most 90% identity with SEQ ID NO: 1.

125. The method of any one of claims 119 to 124, wherein X comprises a sequence having at most 80% identity with SEQ ID NO: 1, X comprises a sequence having at most 70% identity with SEQ ID NO: 1, or X comprises a sequence having at most 50% identity with SEQ ID NO: 1.

126. The method of any one of claims 119 to 125, wherein Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, Y comprises a sequence having at least 95% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2.

127. The method of any one of claims 119 to 126, wherein at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

128. The method of any one of claims 119 to 127, wherein a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10.

129. The method of any one of claims 119 to 128, wherein X comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs:19-22 and 76-79, or X comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 19-22 and 76-79.

130. The method of any one of claims 119 to 129, wherein the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 45-48 and 86-89.

131. The method of claim 119, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

132. The method of claim 119, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

133. The method of claim 119, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

134. The method of claim 119, wherein the peripheral neuropathy is associated with medical condition.

135. The method of claim 134, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

136. The method of claim 135, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

137. The method of claim 135, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

138. The method of claim 137, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

139. The method of claim 135, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

140. The method of claim 135, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

141. The method of claim 119, wherein the peripheral neuropathy is associated with medication.

142. The method of claim 141, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

143. The method of claim 142, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

144. The method of claim 143, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

145. The method of claim 143, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

146. The method of claim 145, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

147. The method of claim 145, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

148. The method of claim 143, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

149. The method of claim 143, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

150. The method of claim 143, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

151. The method of claim 142, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

152. The method of claim 119, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

153. The method of claim 119, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

154. The method of any one of claims 119 to 130, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

155. The method of any one of claims 119 to 130, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

156. The method of any one of claims 119 to 130, wherein the subject does not manifest peripheral neuropathic pain.

157. The method of any one of claims 119 to 130, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

158. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

159. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

160. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

161. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

162. The method of claim 161, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

163. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2.

164. The method of any one of claims 158 to 163, wherein Y comprises 10 to 25 amino acids, Y comprises 10 to 20 amino acids, or Y comprises 10 to 15 amino acids.

165. The method of any one of claims 158 to 164, wherein X comprises a sequence having at least 90% identity with SEQ ID NO: 1, X comprises a sequence having at least 95% identity with SEQ ID NO: 1, or X comprises a sequence of SEQ ID NO: 1.

166. The method of any one of claims 158 to 165, wherein at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H.

167. The method of any one of claims 158 to 166, wherein X comprises a sequence having at least 80% identity with SEQ ID NO: 96, X comprises a sequence having at least 90% identity with SEQ ID NO: 96, X comprises a sequence having at least 95% identity with SEQ ID NO: 96, or X comprises a sequence of SEQ ID NO: 96.

168. The method of any one of claims 158 to 167, wherein Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 50% identity with SEQ ID NO: 2.

169. The method of any one of claims 158 to 168, wherein Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103, Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 97-103, Y comprises a sequence having at least

95% identity with any one selected from SEQ ID NOs: 97-103, or Y comprises a sequence that is any one selected from SEQ ID NOs: 97-103.

170. The method of any one of claims 158 to 169, wherein the polypeptide comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 53-56 and 104-110.

171. The method of claim 158, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

172. The method of claim 158, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

173. The method of claim 158, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

174. The method of claim 158, wherein the peripheral neuropathy is associated with medical condition.

175. The method of claim 174, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

176. The method of claim 175, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

177. The method of claim 175, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

178. The method of claim 177, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

179. The method of claim 175, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

180. The method of claim 175, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

181. The method of claim 158, wherein the peripheral neuropathy is associated with medication.

182. The method of claim 181, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

183. The method of claim 182, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

184. The method of claim 183, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

185. The method of claim 183, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

186. The method of claim 185, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

187. The method of claim 185, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

188. The method of claim 183, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

189. The method of claim 183, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

190. The method of claim 183, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

191. The method of claim 182, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

192. The method of claim 158, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

193. The method of claim 158, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

194. The method of any one of claims 158 to 170, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

195. The method of any one of claims 158 to 170, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

196. The method of any one of claims 158 to 170, wherein the subject does not manifest peripheral neuropathic pain.

197. The method of any one of claims 158 to 170, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

198. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

199. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

200. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

201. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

202. The method of claim 201, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

203. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VI):

X-Y (VI),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in SEQ ID NO: 1 mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in SEQ ID NO: 1 mutated to T; and

Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, or 5 C in SEQ ID NO: 2 mutated to A.

204. The method of any one of claims 198 to 203, wherein X comprises a sequence having at least 70% identity with SEQ ID NO: 1 and/or X comprises a sequence having at most 95% identity with SEQ ID NO: 1.

205. The method of any one of claims 198 to 204, wherein Y comprises a sequence having at least 80% identity with SEQ ID NO: 2 and/or Y comprises a sequence having at most 95% identity with SEQ ID NO: 2.

206. The method of any one of claims 198 to 205, wherein at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

207. The method of any one of claims 198 to 206, wherein a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30 and/or a total number of W, Y, F, M, L, I, and V in X is no more than 20.

208. The method of any one of claims 198 to 207, wherein a total number of R, K, T, A, N, Q, D, E, S, and G in Y is more than 10 and/or a total number of W, Y, F, M, L, I, and V in Y is no more than 20.

209. The method of any one of claims 198 to 208, wherein X comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 80-83, X comprises a sequence that is any one selected from SEQ ID NOs: 80-83, or X is a sequence that is any one selected from SEQ ID NOs: 80-83.

210. The method of any one of claims 198 to 209, wherein Y comprises a sequence having at least 80% identity with SEQ ID NO: 3, Y comprises a sequence of SEQ ID NO: 3, or Y is a sequence of SEQ ID NO: 3.

211. The method of any one of claims 198 to 210, wherein the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 90-93, the artificial polypeptide comprises a sequence that is any one selected from SEQ ID NOs: 90-93, or the artificial polypeptide is a sequence that is any one selected from SEQ ID NOs: 90-93.

212. The method of claim 198, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

213. The method of claim 198, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

214. The method of claim 198, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

215. The method of claim 198, wherein the peripheral neuropathy is associated with medical condition.

216. The method of claim 215, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

217. The method of claim 216, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

218. The method of claim 216, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

219. The method of claim 218, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

220. The method of claim 216, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

221. The method of claim 216, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

222. The method of claim 198, wherein the peripheral neuropathy is associated with medication.

223. The method of claim 222, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

224. The method of claim 223, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

225. The method of claim 224, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

226. The method of claim 224, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

227. The method of claim 226, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

228. The method of claim 226, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

229. The method of claim 224, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

230. The method of claim 224, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

231. The method of claim 224, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

232. The method of claim 223, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

233. The method of claim 198, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

234. The method of claim 198, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

235. The method of any one of claims 198 to 211, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

236. The method of any one of claims 198 to 211, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

237. The method of any one of claims 198 to 211, wherein the subject does not manifest peripheral neuropathic pain.

238. The method of any one of claims 198 to 211, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

239. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

240. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

241. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

242. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

243. The method of claim 242, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

244. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of an artificial polypeptide of formula (VII):

X-Y (VII),

wherein X is a moiety comprising a mutant of the sequence SEQ ID NO: 1, characterized in that the mutant has at least 1, 2, 3, 4, or 5 amino acid insertions relative to SEQ ID NO: 1, and

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 15 continuous AAs of SEQ ID NO: 2.

245. The method of any one of claims 239 to 244, wherein the amino acid insertions are located at the N-terminal of X and/or the inserted amino acid is M.

246. The method of any one of claims 239 to 245, wherein Y is a moiety comprising a mutant of the sequence SEQ ID NO: 2, characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations relative to SEQ ID NO: 2 and optionally the at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid truncations are located at the C-terminal of Y.

247. The method of any one of claims 239 to 246, wherein at least 50% amino acids of X are selected from R, K, N, D, Q, E, and H and/or at most 60% amino acids of X are selected from R, K, N, D, Q, E, and H.

248. The method of any one of claims 239 to 247, wherein a total number of E or D in X is at least 8 and/or a total number of E or D in X is at most 15.

249. The method of any one of claims 239 to 248, wherein a total number of R, K, T, A, N, Q, D, E, S, and G in X is more than 30 and/or a total number of W, Y, F, M, L, I, and V in X is no more than 20.

250. The method of any one of claims 239 to 249, wherein Y comprises 15 to 25 amino acids, Y comprises 18 to 25 amino acids, or Y comprises 20 to 25 amino acids.

251. The method of any one of claims 239 to 250, wherein 40-65% amino acids of Y are selected from I, V, L, F, C, M, and A.

252. The method of any one of claims 239 to 251, wherein a total number of R, K, T, A, N, Q, D, E, S, and G in Y is no more than 10 and/or a total number of W, Y, F, M, L, I, and V in Y is no more than 15.

253. The method of any one of claims 239 to 252, wherein X comprises a sequence having at least 80% identity with SEQ ID NO: 96, X comprises a sequence of SEQ ID NO: 96, or X is a sequence of SEQ ID NO: 96.

254. The method of any one of claims 239 to 253, wherein Y comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 97-103, Y comprises a sequence that is any one selected from SEQ ID NOs: 97-103, or Y is a sequence that is any one selected from SEQ ID NOs: 97-103.

255. The method of any one of claims 239 to 254, wherein the artificial polypeptide comprises a sequence having at least 80% identity with any one selected from SEQ ID NOs: 104-110, the artificial polypeptide comprises a sequence that is any one selected from SEQ ID NOs: 104-110, or the artificial polypeptide is a sequence that is any one selected from SEQ ID NOs: 104-110.

256. The method of claim 239, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

257. The method of claim 239, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

258. The method of claim 239, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

259. The method of claim 239, wherein the peripheral neuropathy is associated with medical condition.

260. The method of claim 259, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury,

demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

261. The method of claim 260, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

262. The method of claim 260, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

263. The method of claim 262, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

264. The method of claim 260, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

265. The method of claim 260, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

266. The method of claim 239, wherein the peripheral neuropathy is associated with medication.

267. The method of claim 266, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

268. The method of claim 267, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

269. The method of claim 268, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

270. The method of claim 268, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

271. The method of claim 270, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

272. The method of claim 270, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

273. The method of claim 268, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

274. The method of claim 268, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

275. The method of claim 268, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

276. The method of claim 267, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

277. The method of claim 239, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

278. The method of claim 239, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

279. The method of any one of claims 239 to 255, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

280. The method of any one of claims 239 to 255, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

281. The method of any one of claims 239 to 255, wherein the subject does not manifest peripheral neuropathic pain.

282. The method of any one of claims 239 to 255, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

283. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

284. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

285. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

286. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

287. The method of claim 286, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

288. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (I):

X-Y (I),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a total number of Cysteine (C) of less than 5,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

289. The method of any one of claims 283 to 288, wherein at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H.

290. The method of any one of claims 283 to 289, wherein X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

291. The method of any one of claims 283 to 290, wherein Y comprises a total number of Cysteine (C) of less than 4, or Y comprises a total number of Cysteine (C) of less than 3.

292. The method of any one of claims 283 to 291, wherein a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5.

293. The method of any one of claims 283 to 292, wherein Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-15, 58-61 and 84-85, or Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 3-18, 58-61 and 84-85.

294. The method of claim 283, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

295. The method of claim 283, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

296. The method of claim 283, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

297. The method claim 283, wherein the peripheral neuropathy is associated with medical condition.

298. The method of claim 297, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

299. The method of claim 298, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

300. The method of claim 298, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

301. The method of claim 300, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

302. The method of claim 298, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

303. The method of claim 298, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

304. The method of claim 283, wherein the peripheral neuropathy is associated with medication.

305. The method of claim 304, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

306. The method of claim 305, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

307. The method of claim 306, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

308. The method of claim 306, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

309. The method of claim 308, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

310. The method of claim 308, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

311. The method of claim 306, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

312. The method of claim 306, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

313. The method of claim 306, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

314. The method of claim 305, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

315. The method of claim 283, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

316. The method of claim 283, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

317. The method of any one of claims 283 to 293, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

318. The method of any one of claims 283 to 293, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

319. The method of any one of claims 283 to 293, wherein the subject does not manifest peripheral neuropathic pain.

320. The method of any one of claims 283 to 293, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

321. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

322. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

323. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

324. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

325. The method of claim 324, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

326. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (II):

X-Y (II),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 50 amino acids, at least 50% of which are selected from I, V, L, F, C, M, and A,

Y comprises a sequence having at most 90% identity with SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

327. The method of any one of claims 321 to 326, wherein at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H.

328. The method of any one of claims 321 to 327, wherein X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

329. The method of any one of claims 321 to 328, wherein Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 70% identity with SEQ ID NO: 2.

330. The method of any one of claims 321 to 329, wherein a total number of hydrophobic amino acids in Y is more than 8, the total number of hydrophobic amino acids in Y is more than 12, the total

number of hydrophobic amino acids in Y is more than 15, and/or a total number of hydrophilic amino acids in Y is no more than 5.

331. The method of any one of claims 321 to 330, wherein Y comprises a sequence having at least 90% identity with any one selected from SEQ ID NOs: 16-18, or Y comprises a sequence having at least 95% identity with any one selected from SEQ ID NOs: 16-18.

332. The method of claim 321, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

333. The method of claim 321, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

334. The method of claim 321, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

335. The method of claim 321, wherein the peripheral neuropathy is associated with medical condition.

336. The method of claim 335, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

337. The method of claim 336, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

338. The method of claim 336, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

339. The method of claim 338, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

340. The method of claim 336, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

341. The method of claim 336, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

342. The method of claim 321, wherein the peripheral neuropathy is associated with medication.

343. The method of claim 342, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

344. The method of claim 343, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

345. The method of claim 344, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

346. The method of claim 344, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

347. The method of claim 346, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

348. The method of claim 346, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

349. The method of claim 344, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

350. The method of claim 344, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

351. The method of claim 344, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

352. The method of claim 343, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

353. The method of claim 321, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

354. The method of claim 321, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

355. The method of any one of claims 321 to 331, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

356. The method of any one of claims 321 to 331, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

357. The method of any one of claims 321 to 331, wherein the subject does not manifest peripheral neuropathic pain.

358. The method of any one of claims 321 to 331, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

359. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

360. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

361. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

362. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

363. The method of claim 362, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

364. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (III):

X-Y (III),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

a total number of H, R, K, D, Q, N and E in X is less than 33,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

365. The method of any one of claims 359 to 364, wherein at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H.

366. The method of any one of claims 359 to 365, wherein X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

367. The method of any one of claims 359 to 366, wherein Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2.

368. The method of any one of claims 359 to 367, wherein at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

369. The method of any one of claims 359 to 368, wherein the total number of H, R, K, D, Q, N and E in X is less than 30, the total number of H, R, K, D, Q, N and E in X is less than 25, or the total number of H, R, K, D, Q, N and E in X is less than 20.

370. The method of any one of claims 359 to 369, wherein a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10.

371. The method of claim 359, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

372. The method of claim 359, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

373. The method of claim 359, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

374. The method of claim 359, wherein the peripheral neuropathy is associated with medical condition.

375. The method of claim 374, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

376. The method of claim 375, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

377. The method of claim 375, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

378. The method of claim 377, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

379. The method of claim 375, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

380. The method of claim 375, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

381. The method of claim 359, wherein the peripheral neuropathy is associated with medication.

382. The method of claim 381, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

383. The method of claim 382, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

384. The method of claim 383, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

385. The method of claim 383, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

386. The method of claim 385, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

387. The method of claim 385, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

388. The method of claim 383, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

389. The method of claim 383, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

390. The method of claim 383, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

391. The method of claim 382, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

392. The method of claim 359, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

393. The method of claim 359, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

394. The method of any one of claims 359 to 370, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

395. The method of any one of claims 359 to 370, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

396. The method of any one of claims 359 to 370, wherein the subject does not manifest peripheral neuropathic pain.

397. The method of any one of claims 359 to 370, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

398. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

399. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

400. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

401. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

402. The method of claim 401, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

403. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (IV):

X-Y (IV),

wherein X is a moiety comprising 40 to 65 amino acids, at least 50% of which are selected from H, R, K, D, Q, N and E,

Y is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 2,

X comprises a sequence having at most 90% identity with SEQ ID NO: 1,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

404. The method of any one of claims 398 to 403, wherein at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H.

405. The method of any one of claims 398 to 404, wherein X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

406. The method of any one of claims 398 to 405, wherein Y comprises a sequence having at least 90% identity with SEQ ID NO: 2, or Y comprises a sequence of SEQ ID NO: 2.

407. The method of any one of claims 398 to 406, wherein at least 50% amino acids of Y are selected from I, V, L, F, C, M, and A.

408. The method of any one of claims 398 to 407, wherein a total number of hydrophilic amino acids in X is more than 10, a total number of hydrophilic amino acids in X is more than 15, a total number of hydrophilic amino acids in X is more than 20, a total number of hydrophilic amino acids in X is more than 25, a total number of hydrophobic amino acids in X is no more than 15, and/or the total number of hydrophobic amino acids in X is no more than 10.

409. The method of claim 398, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

410. The method of claim 398, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

411. The method of claim 398, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

412. The method of claim 398, wherein the peripheral neuropathy is associated with medical condition.

413. The method of claim 412, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular

atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

414. The method of claim 413, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

415. The method of claim 413, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

416. The method of claim 415, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

417. The method of claim 413, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

418. The method of claim 413, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

419. The method of claim 398, wherein the peripheral neuropathy is associated with medication.

420. The method of claim 419, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

421. The method of claim 420, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

422. The method of claim 421, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

423. The method of claim 421, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

424. The method of claim 423, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

425. The method of claim 423, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

426. The method of claim 421, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

427. The method of claim 421, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

428. The method of claim 421, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

429. The method of claim 420, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

430. The method of claim 398, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

431. The method of claim 398, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

432. The method of any one of claims 398 to 408, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

433. The method of any one of claims 398 to 408, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

434. The method of any one of claims 398 to 408, wherein the subject does not manifest peripheral neuropathic pain.

435. The method of any one of claims 398 to 408, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

436. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

437. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

438. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

439. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

440. The method of claim 439, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

441. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a mutant of artificial polypeptide of formula (V):

X-Y (V),

wherein X is a moiety comprising a sequence having at least 80% identity with SEQ ID NO: 1,

Y is a moiety comprising 10 to 30 amino acids, wherein Y comprises a sequence having at least 10 continuous AAs of SEQ ID NO: 2,

characterized in that the mutant has at least 1, 2, 3, 4, 5, 6, 7, 8, or 9 D in X mutated to S, and/or at least 1, 2, 3, 4, 5, or 6 E in X mutated to T.

442. The method of any one of claims 436 to 441, wherein at least 20% amino acids of X are selected from R, K, N, D, Q, E, and H, at least 30% amino acids of X are selected from R, K, N, D, Q, E, and H, at most 90% amino acids of X are selected from R, K, N, D, Q, E, and H, and/or at most 80% amino acids of X are selected from R, K, N, D, Q, E, and H.

443. The method of any one of claims 436 to 442, wherein Y comprises 10 to 25 amino acids, Y comprises 10 to 20 amino acids, or Y comprises 10 to 15 amino acids.

444. The method of any one of claims 436 to 443, wherein X comprises a sequence having at least 70% identity with SEQ ID NO: 1.

445. The method of any one of claims 436 to 444, wherein Y comprises a sequence having at most 80% identity with SEQ ID NO: 2, Y comprises a sequence having at most 70% identity with SEQ ID NO: 2, or Y comprises a sequence having at most 50% identity with SEQ ID NO: 2.

446. The method of claim 436, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

447. The method of claim 436, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

448. The method of claim 436, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

449. The method of claim 436, wherein the peripheral neuropathy is associated with medical condition.

450. The method of claim 449, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

451. The method of claim 450, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

452. The method of claim 450, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

453. The method of claim 452, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

454. The method of claim 450, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

455. The method of claim 450, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

456. The method of claim 436, wherein the peripheral neuropathy is associated with medication.

457. The method of claim 456, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

458. The method of claim 457, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

459. The method of claim 458, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

460. The method of claim 458, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

461. The method of claim 460, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

462. The method of claim 460, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

463. The method of claim 458, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

464. The method of claim 458, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

465. The method of claim 458, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

466. The method of claim 457, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

467. The method of claim 436, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

468. The method of claim 436, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

469. The method of any one of claims 436 to 445, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

470. The method of any one of claims 436 to 445, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

471. The method of any one of claims 436 to 445, wherein the subject does not manifest peripheral neuropathic pain.

472. The method of any one of claims 436 to 445, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.

473. A method for preventing and/or treating peripheral neuropathy or nerve injury associated with peripheral neuropathy in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

474. A method for effecting and/or promoting neuroprotection and/or neuroregeneration in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

475. A method for alleviating and/or mitigating cell damage and/or inflammatory response of nervous tissues or nerve cells in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

476. A method for improving nerve conduction velocity in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

477. The method of claim 476, wherein the nerve conduction velocity is motor conduction velocity, sensory conduction velocity or both.

478. A method for increasing intraepidermal nerve fiber density in a subject in need thereof, comprising administering to the subject an effective amount of a polypeptide having at least 70% identity with any one selected from SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof.

479. The method of any one of claims 473 to 478, wherein the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74 or a fragment or variant thereof, the polypeptide is a polypeptide of any one of SEQ ID NO: 28, SEQ ID NOs: 57 and 62-74, the polypeptide is a polypeptide of any one of SEQ ID NOs: 28 and 62-74, or the polypeptide is a polypeptide of SEQ ID NO: 28.

480. The method of claim 473, wherein the peripheral neuropathy is one or more selected from the group consisting of mononeuropathy, mononeuritis multiplex and polyneuropathy.

481. The method of claim 473, wherein the peripheral neuropathy is one or more selected from the group consisting of motor neuropathy, sensory neuropathy and autonomic neuropathy.

482. The method of claim 473, wherein the peripheral neuropathy is associated with one or more selected from the group consisting of medical condition, compression, traumatic injury, medication, exposure to toxic chemical agents, radiation therapy, excessive alcohol consumption and vitamin deficiency.

483. The method of claim 473, wherein the peripheral neuropathy is associated with medical condition.

484. The method of claim 483, wherein the medical condition is one or more selected from the group consisting of diabetes, inflammation, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), post-polio syndrome, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, muscular dystrophy, peripheral nerve injury, demyelination, adrenoleukodystrophy, kidney disease, liver disease, Parkinson's disease, stroke, Alzheimer's disease, infection, tumor, carpal tunnel syndrome, post-herpetic neuralgia, peroneal muscular atrophy, Fabry disease, severe polyneuropathy, Bell's palsy, ulnar nerve palsy, peroneal nerve palsy, ischemia, immune system disease, non-celiac gluten sensitivity, sarcoidosis and cryoglobulinemia.

485. The method of claim 484, wherein the inflammation is one or more selected from the group consisting of acute disseminated leukoencephalitis, progressive multifocal leukoencephalitis (PML), optic neuritis, transverse myelitis and vasculitis.

486. The method of claim 484, wherein the infection is one or more selected from the group consisting of leprosy, lyme disease and viral infection.

487. The method of claim 486, wherein the viral infection is one or more selected from the group consisting of parvovirus B19 infection and HIV infection.

488. The method of claim 484, wherein the tumor is one or more selected from the group consisting of lymphoma, neurilemmoma and multiple myeloma.

489. The method of claim 484, wherein the immune system disease is one or more selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis and celiac disease.

490. The method of of claim 473, wherein the peripheral neuropathy is associated with medication.

491. The method of claim 490, wherein the medication is treatment with chemotherapeutic agent and/or antibiotic.

492. The method of claim 491, wherein the chemotherapeutic agent is one or more selected from the group consisting of platinum-based antineoplastic drug, microtubule inhibitor, topoisomerase II inhibitor, immunomodulator, proteasome inhibitor and suramin.

493. The method of claim 492, wherein the platinum-based antineoplastic drug is one or more selected from the group consisting of cisplatin, oxaliplatin, carboplatin, nedaplatin, dicycloplatin, lobaplatin, eptaplatin, miriplatin, picoplatin, satraplatin and triplatin tetranitrate.

494. The method of claim 492, wherein the microtubule inhibitor is one or more selected from the group consisting of taxoid, Vinca alkaloid, ixabepilone and eribulin.

495. The method of claim 494, wherein the taxoid is one or more selected from the group consisting of paclitaxel, docetaxel and cabazitaxel.

496. The method of claim 494, wherein the Vinca alkaloid is one or more selected from the group consisting of vinblastine, vincristine, vindesine, vinorelbine, vincaminol, vineridine and vinburnine.

497. The method of claim 492, wherein the Topoisomerase II inhibitor is one or more selected from the group consisting of etoposide, teniposide, doxorubicin, daunorubicin, epirubicin and idarubicin.

498. The method of claim 492, wherein the immunomodulator is one or more selected from the group consisting of thalidomide, lenalidomide and pomalidomide.

499. The method of claim 492, wherein the proteasome inhibitor is one or more selected from the group consisting of bortezomib, carfilzomib, ixazomib, marizomib, oprozomib and delanzomib.

500. The method of claim 491, wherein the antibiotic is one or more selected from the group consisting of metronidazole, ciprofloxacin, levofloxacin and moxifloxacin.

501. The method of claim 473, wherein the peripheral neuropathy is diabetic peripheral neuropathy or chemotherapy-induced peripheral neuropathy (CIPN).

502. The method of claim 473, wherein the nerve injury associated with peripheral neuropathy is one or more selected from the group consisting of impaired nerve cells, impaired nerve fibers and impaired nerve conduction.

503. The method of any one of claims 473 to 479, wherein the subject is afflicted by peripheral neuropathy or is in the risk of developing peripheral neuropathy.

504. The method of any one of claims 473 to 479, wherein the subject does not manifest pain attributable to peripheral neuropathy or nerve injury associated with peripheral neuropathy.

505. The method of any one of claims 473 to 479, wherein the subject does not manifest peripheral neuropathic pain.

506. The method of any one of claims 473 to 479, wherein the subject manifests or is in the risk of developing one or more symptoms associated with peripheral neuropathy, wherein the symptoms associated with peripheral neuropathy are selected from the group consisting of inability to feel heat, cold and/or physical damage; numbness; hypersensitivity to touch; loss of coordination and/or proprioception; muscle weakness; muscle atrophy; muscle twitches; cramps; and muscle paralysis.