A further specific object of this invention is a method of restoring axon morphology, growth or electrophysiological function in a subject in need thereof, the method comprising administering to said subject an effective amount of a compound or combination of compounds as disclosed above

The invention is particularly suited to treat subjects having neuropraxia, axonotmesis, or neurotmesis, as well as in subjects having a traumatic brain injury, spinal cord injury, or a mechanical injury of peripheral nerves.

Any of the various uses or methods of treatment disclosed herein can also include an optional step of diagnosing a patient as having the mechanical insult.

In this regard, a further object of this invention is a method of treating a mechanical nerve injury, the method comprising (1) assessing whether a subject has mechanical nerve injury and (2) treating the subject having mechanical nerve injury with an effective amount of a combination of compounds as described above, said treatment resulting in nerve regeneration. Determining whether a subject has mechanical nerve injury can be done by various tests known per se in the art.

The invention may be used in any mammalian subject, particularly human subjects.

Legend to the figures

Figure 1. Synergistic effect of drug combination, dose 1: effect of **A)** Mix7 (dose 1, day 10), **B)** D-Sorbitol (SRB, 500 µM, day 10), **C)** (R/S)-Baclofen (BCL, 5 µM, day 10) and **D)** Naltrexone (NTX, 5 µM, day 10) on MBP expression. *:$p<0.05$: significantly different from control (=ascorbic acid) (One-Way ANOVA followed by Fisher Post-hoc test); ns: not statistically different.

Figure 2. Synergistic effect of drug combination, dose 6 **A)** Mix7 (dose 6, day 10), **B)** SRB (160 nM, day 10), **C)** BCL (1.6 nM, day 10) and **D)** NTX (1.6 nM, day 10) on MBP expression. *:$p<0.05$: significantly different from control (=ascorbic acid) (One-Way ANOVA followed by Fisher Post-hoc test); ns: not statistically different.

neuronal insult), prion-based neurodegeneration, including Creutzfeld-Jakob disease (CJD), bovine spongiform encephalopathy (BSE), GSS, FFI, Kuru and Alper's syndrome.

In a preferred embodiment, "CMT related disorder" designates a toxic or traumatic neuropathy, particularly drug-induced neuropathies, ALS or neuropathies resulting from a mechanical neuronal insult.

Within the context of the invention, "mechanical neuronal insults" refers to a direct physical damage to the nerve either in the central nervous system (CNS) or in the peripheral nervous system (PNS). Damages to the PNS can be ranked according to the stage of the neuronal insult. The present invention is suited for treating nerve injuries ranking from neuropraxia (condition where only signalling ability of the nerve is impaired), axonotmesis (injury implying damages to the axons, without impairing surrounding connective tissues of the nerves), and also neurotmesis (injury damaging both axon and surrounding tissues). Mechanical neuronal insults can have accidental origin, or result from surgery or from other conditions like, for example, childbirth associated urinary incontinence.

Damages to the CNS encompass spinal cord injuries as well as traumatic brain injuries. Traumatic brain injuries can be either primary (i.e., resulting directly from the trauma) or secondary injuries (i.e., which are the consequences of the trauma). Spinal cord injuries can be ranked according the extent of sensory and motor disabilities, as set up in the *International Standards for Neurological Classification of Spinal Cord Injury* (Kirshblum *et al.*, 2011).

As used herein, "treatment" of a disorder includes the therapy, prevention, prophylaxis retardation or reduction of pain provoked by the disorder. The term treatment includes in particular the control of disease progression and associated symptoms. In particular, the treatment of a CMT or related neuropathy according to the invention includes a prevention or retardation or reduction or improvement in a motor, autonomic and/or sensory impairment caused by such diseases. Motor symptoms include uncontrollable contraction, fasciculation weakness, or complete

Claims

1. Use of a combination comprising baclofen, sorbitol and a compound selected from pilocarpine, methimazole, mifepristone, naltrexone, rapamycin, flurbiprofen, or ketoprofen, or salts, enantiomers or racemates thereof, in the manufacture of a medicament for promoting or improving nerve regeneration in a subject suffering from a traumatic neuropathy or a mechanical neuronal insult.

2. The use of claim 1, wherein the combination comprises baclofen, D-sorbitol and naltrexone, or salts, enantiomers or racemates thereof.

3. The use of claim 1 or 2, further comprising a pharmaceutically suitable excipient or carrier.

4. The use of any one of claims 1 to 3, wherein the compounds are formulated with a drug eluting polymer, a biomolecule, a micelle or liposome-forming lipids or oil in water emulsions, or pegylated or solid nanoparticles or microparticles for oral or parenteral or intrathecal administration.

5. The use of any one of the preceding claims, wherein the compounds are formulated to be administered together or separately, simultaneously or sequentially.

6. The use of any one of claims 1 to 5, wherein improving nerve regeneration comprises improving or accelerating recovery from said neuronal insult or traumatic neuropathy.

7. The use of any one of claims 1 to 5, wherein improving nerve regeneration comprises improving nerve myelination or restoring, at least partially, axon morphology, axon growth or electrophysiological functions.

8. The use of any one of claims 1 to 7, wherein the mechanical neuronal insult is neuropraxia, axonotmesis, or neurotmesis.

9. The use of any one of claims 1 to 7, wherein the mechanical neuronal insult consists in traumatic brain injury, spinal cord injury, or a mechanical injury of peripheral nerves.