

CLAIMS

1. A method of promoting survival and/or function of an amyotrophic lateral sclerosis (ALS) or ALS-like motor neuron, the method comprising
5 contacting the motor neuron with an agent capable of reducing mitochondrial protein acetylation.
2. The method of claim 1, wherein the agent is selected from the group consisting of: a deacetylase activator, an acetyltransferase inhibitor and
10 combinations thereof.
3. The method of claim 2, wherein the deacetylase activator comprises a SIRT3 (Sirtuin 3) activator.
- 15 4. The method of claim 3, wherein the SIRT3 activator is selected from the group consisting of: a small molecule, a NAD (nicotinamide adenine dinucleotide) or a precursor thereof, and combinations thereof.
- 20 5. The method of claim 4, wherein the small molecule is selected from the group consisting of: 7-hydroxy-3-(4'-methoxyphenyl) coumarin (C12), honokiol, dihydromyricetin (DHM) and derivatives, analogues and combinations thereof.
- 25 6. The method of claim 4, wherein the NAD precursor is selected from the group consisting of tryptophan, quinolinic acid, nicotinic acid (NA), nicotinamide (Nam), nicotinamide mononucleotide (NMN) nicotinamide riboside (NR), nicotinic acid and derivatives, analogues and combinations thereof.
- 30 7. The method of claim 2, wherein the acetyltransferase inhibitor comprises a GCN5L1 (GCN5 (general control of amino acid synthesis 5)-like 1) inhibitor.

8. The method of claim 7, wherein the GCN5L1 inhibitor comprises an oligonucleotide.
9. The method of claim 8, wherein the oligonucleotide is selected from the group consisting of: antisense oligonucleotide (ASO), gapmer, short interfering RNA (siRNA), short hairpin RNA (shRNA), microRNA (miRNA), guide RNA (gRNA), single guide RNA (sgRNA) and combinations thereof.
10. The method of claim 8 or claim 9, wherein the oligonucleotide comprises:
- a) a sequence that is complementary to a coding sequence (CDS) of *BLOC1S1* gene or part thereof, or SEQ ID NO: 3 or part thereof, or SEQ ID NO: 4 or part thereof; or
 - b) a sequence sharing at least about 75% sequence identity with the sequence in a).
11. The method of any one of claims 8 to 10, wherein the oligonucleotide comprises a sequence sharing at least about 75% sequence identity with SEQ ID NO: 1, or a sequence differing from SEQ ID NO: 1 by about one nucleotide, about two nucleotides, about three nucleotides, about four nucleotides or about five nucleotides.
12. An agent capable of reducing mitochondrial protein acetylation for use in treating ALS or an ALS-like disease.
13. The agent of claim 12, wherein the agent is selected from the group consisting of: a deacetylase activator, an acetyltransferase inhibitor and combinations thereof.
14. The agent of claim 13, wherein the deacetylase activator comprises a SIRT3 activator, optionally wherein the SIRT3 activator is selected from the group consisting of: a small molecule, a NAD or a precursor thereof, and combinations thereof, optionally wherein the small molecule is selected from the group consisting of: C12, honokiol, dihydromyricetin

(DHM) and derivatives, analogues and combinations thereof, optionally wherein the NAD precursor is selected from the group consisting of tryptophan, quinolinic acid, nicotinic acid (NA), nicotinamide (Nam), nicotinamide mononucleotide (NMN) nicotinamide riboside (NR), nicotinic acid and derivatives, analogues and combinations thereof.

15. The agent of claim 13, wherein the acetyltransferase inhibitor comprises GCN5L1 inhibitor, optionally wherein the GCN5L1 inhibitor comprises an oligonucleotide, optionally wherein the oligonucleotide is selected from the group consisting of: antisense oligonucleotide (ASO), gapmer, short interfering RNA (siRNA), short hairpin RNA (shRNA), microRNA (miRNA), guide RNA (gRNA), single guide RNA (sgRNA) and combinations thereof, optionally wherein the oligonucleotide comprises: a) a sequence that is complementary to a CDS of *BLOC1S1* gene or part thereof, or SEQ ID NO: 3 or part thereof, or SEQ ID NO: 4 or part thereof; or a sequence sharing at least about 75% sequence identity with the sequence in a), optionally wherein the oligonucleotide comprises a sequence sharing at least about 75% sequence identity with SEQ ID NO: 1, or a sequence differing from SEQ ID NO: 1 by about one nucleotide, about two nucleotides, about three nucleotides, about four nucleotides or about five nucleotides.

16. Use of the agent of any one of claim 12 to 15 in the manufacture of a medicament for treating ALS or an ALS-like disease.

17. A method of treating ALS or an ALS-like disease in a subject, the method comprising administering to the subject the agent of any one of claim 12 to 15.

18. An oligonucleotide sharing at least about 75% sequence identity with SEQ ID NO: 1, or a sequence differing from SEQ ID NO: 1 by about one

nucleotide, about two nucleotides, about three nucleotides, about four nucleotides or about five nucleotides.

19. The oligonucleotide of claim 18 for use in therapy.

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20. A method of identifying an agent for treating ALS or an ALS-like disease, the method comprising:

contacting an ALS or ALS-like motor neuron with a candidate agent;

and

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determining whether mitochondrial protein acetylation in the motor neuron is reduced after the contact; and

wherein where mitochondrial protein acetylation in the motor neuron is reduced after the contact, concluding that the candidate agent is an agent for treating ALS or an ALS-like disease,

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wherein where mitochondrial protein acetylation in the motor neuron is not reduced after the contact, concluding that the candidate agent is not an agent for treating ALS or an ALS-like disease,

optionally wherein the agent for treating ALS or an ALS-like disease so identified comprises an agent according to claims 12 to 15, or an oligonucleotide according to claims 18 or 19.

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