~~**Claims**~~

~~1. A LINC complex inhibitor for use in a method of treating or preventing a laminopathy.~~

~~2. Use of a LINC complex inhibitor in the manufacture of a medicament for use in a method of treating or preventing a laminopathy.~~

~~3. A method of treating or preventing a laminopathy, comprising administering a therapeutically or prophylactically effective amount of a LINC complex inhibitor to a subject.~~

~~4. The LINC complex inhibitor for use according to claim 1, the use according to claim 2, or the method according to claim 3, wherein the laminopathy is characterised by one or more of myopathy, cardiomyopathy, dilated cardiomyopathy, muscular dystrophy, cardiac muscular dystrophy, skeletal muscular dystrophy, progeria, neuropathy, lipoatrophy, skeletal dysplasia, lipodystrophy, leukodystrophy ordermopathy.~~

~~5. The LINC complex inhibitor for use, the use or the method according to any one of claims 1 to 4, wherein the laminopathy is associated with mutation to LMNA.~~

~~6. The LINC complex inhibitor for use, the use or the method according to any one of claims 1 to 5, wherein the laminopathy is selected from: Hutchinson-Gilford Progeria Syndrome; Dilated Cardiomyopathy; Muscular Dystrophy, Congenital, Lmna-Related; Emery-Dreifuss Muscular Dystrophy 2, Autosomal Dominant; Muscular Dystrophy; Mandibuloacral Dysplasia with Type a Lipodystrophy; Cardiomyopathy, Dilated, 1a; Charcot-Marie-Tooth Disease; Limb-Girdle Muscular Dystrophy; Cardiomyopathy, Dilated, with Hypergonadotropic Hypogonadism; Emery-Dreifuss Muscular Dystrophy 3, Autosomal Recessive; Lipodystrophy, Familial Partial, Type 2; Emery-Dreifuss Muscular Dystrophy; Charcot-Marie-Tooth Disease, Axonal, Type 2b1 ; Heart-Hand Syndrome, Slovenian Type; Aging; Familial Partial Lipodystrophy; Restrictive Dermopathy, Lethal; Arrhythmogenic Right Ventricular Cardiomyopathy; Tooth Disease; Heart Disease; Werner Syndrome; Hypertrophic Cardiomyopathy; Left Ventricular Noncompaction; Atrioventricular Block; Calcinosis; Acroosteolysis; Autosomal Dominant Limb-Girdle Muscular Dystrophy; Diabetes Mellitus, Noninsulin-Dependent; Osteoporosis; Atrial Fibrillation; Atrial Standstill 1 ; Acanthosis Nigricans; Cardiac Conduction Defect; Catecholaminergic Polymorphic Ventricular Tachycardia; Mandibular Hypoplasia, Deafness, Progeroid Features, and~~

Lipodystrophy Syndrome; Sick Sinus Syndrome; Pelger-Huet Anomaly; Charcot-Marie-Tooth Disease, Axonal, Type 2e; Congenital Generalized Lipodystrophy; Restrictive Cardiomyopathy; Congenital Fiber-Type Disproportion; Lipodystrophy, Congenital Generalized, Type 1 ; Myofibrillar Myopathy; Lipodystrophy, Familial Partial, Type 1 ; Axonal Neuropathy; Atypical Werner Syndrome; Ovarian Cystadenoma; Fanconi Anemia, Complementation Group a; Body Mass Index Quantitative Trait Locus 11 ; Skin Disease; Rigid Spine Muscular Dystrophy 1 ; Neuromuscular Disease; Hallermann-Streiff Syndrome; Bethlem Myopathy 1 ; Acquired Generalized Lipodystrophy; Cardiomyopathy, Dilated, 1e; Lipodystrophy, Congenital Generalized, Type 4; Undifferentiated Pleomorphic Sarcoma; Lipodystrophy, Familial Partial, Type 3; Muscular Dystrophy, Congenital Merosin-Deficient, 1a; Proximal Spinal Muscular Atrophy; Muscular Dystrophy-Dystroglycanopathy , Type B, 5; Muscular Dystrophy, Congenital, 1b; Reynolds Syndrome; Wiedemann-Rautenstrauch Syndrome; Emery-Dreifuss Muscular Dystrophy 1 , X-Linked; Lipodystrophy, Congenital Generalized, Type 2; Monogenic Diabetes; Cardiomyopathy, Dilated, 1d; Myopathy, Proximal, and Ophthalmoplegia; Muscle Tissue Disease; Lipodystrophy, Familial Partial, Type 4; Cardiomyopathy, Dilated, 1 h; Second-Degree Atrioventricular Block; Median Neuropathy; Intrinsic Cardiomyopathy; Prolapse of Female Genital Organ; Complete Generalized Lipodystrophy; Rigid Spine Muscular Dystrophy; Emerinopathy; Ulnar Nerve Lesion; Limb-Girdle Muscular Dystrophy Type 1b; Lmna-Related Dilated Cardiomyopathy; Pelvic Muscle Wasting; Generalized Lipodystrophy-Associated Progeroid Syndrome; Muscular Disease; Cardiomyopathy, Dilated, 1b; Autosomal Genetic Disease; Familial Isolated Arrhythmogenic Ventricular Dysplasia, Right Dominant Form; Familial Isolated Arrhythmogenic Ventricular Dysplasia, Biventricular Form; Familial Isolated Arrhythmogenic Ventricular Dysplasia, Left Dominant Form; Lmna-Related Cardiocutaneous Progeria Syndrome; and Autosomal Semi-Dominant Severe Lipodystrophic Laminopathy.

7. A LINC complex inhibitor for use in a method of treating or preventing a disease characterised by hyperlipidemia.

8. Use of a LINC complex inhibitor in the manufacture of a medicament for use in a method of treating or preventing a disease characterised by hyperlipidemia.

9. A method of treating or preventing a disease characterised by hyperlipidemia, comprising administering a therapeutically or prophylactically effective amount of a LINC complex inhibitor to a subject.

10. The LINC complex inhibitor for use according to claim 7, the use according to claim 8, or the method according to claim 9, wherein the disease characterised by hyperlipidemia is selected from atherosclerosis, cardiovascular disease, stroke and a familial hyperlipidemia.

11. The LINC complex inhibitor for use, the use or the method according to any one of claims 1 to 10, wherein the LINC complex inhibitor is capable of binding to a LINC complex, a LINC complex protein or an interaction partner for a LINC complex protein, or wherein the LINC complex inhibitor is capable of reducing expression of a LINC complex protein.

12. The LINC complex inhibitor for use, the use or the method according to claim 11, wherein the LINC complex inhibitor is capable of inhibiting interaction between a LINC complex protein and an interaction partner for a LINC complex protein.

13. The LINC complex inhibitor for use, the use or the method according to any one of claims 11 or claim 12, wherein the LINC complex inhibitor is a peptide/polypeptide, nucleic acid or small molecule.

14. The LINC complex inhibitor for use, the use or the method according to claim 11, wherein the LINC complex inhibitor is capable of modifying a gene encoding a LINC complex protein to reduce its expression.

15. The LINC complex inhibitor for use, the use or the method according to claim 14, wherein the LINC complex inhibitor comprises a site-specific nuclease (SSN) targeting a gene encoding a LINC complex protein.

16. The LINC complex inhibitor for use, the use or the method according to claim 11, wherein the LINC complex inhibitor is an inhibitory nucleic acid capable of reducing expression of a LINC complex protein by RNA interference (RNAi).

17. The LINC complex inhibitor for use, the use or the method according to any one of claims 11 to 16, wherein the method comprises administering nucleic acid encoding the LINC complex inhibitor, or nucleic acid encoding factors required for production of the LINC complex inhibitor, to the subject.

Claims

1. A nucleic acid encoding a LINC complex inhibitor, wherein the LINC complex inhibitor consists of:

(a) (i) an amino acid sequence having at least 70% amino acid sequence identity to the amino acid sequence of SEQ ID NO:115 or SEQ ID NO:116, and (ii) an endoplasmic reticulum retention motif; or

(b) (i) a signal peptide, (ii) an amino acid sequence having at least 70% amino acid sequence identity to the amino acid sequence of SEQ ID NO:115 or SEQ ID NO:116, and (iii) an endoplasmic reticulum retention motif.

2. The nucleic acid according to claim 1, wherein the LINC complex inhibitor comprises an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence of SEQ ID NO:115.

3. The nucleic acid according to claim 1 or claim 2, wherein the endoplasmic reticulum retention motif is a KDEL motif, or a variant thereof selected from CDEL, KCEL and HVEL.

4. A vector comprising the nucleic acid of any one of claims 1 to 3.

5. The vector according to claim 4, wherein the vector is an adeno-associated viral vector.

6. The vector according to claim 4 or claim 5, wherein the vector is an adeno-associated viral vector selected from one of the following serotypes: AAV9, AAV1, AAV6, AAV8, AAV2i8, AAV9.45, AAV10 and AAVrh.74.

7. The vector according to any one of claims 4 to 6, wherein the vector comprises a promoter providing for expression of the nucleic acid in cardiac and/or skeleteal muscle cells or tissue.

8. The vector according to claim 7, wherein the promoter is a cardiac or cardiomyocte-specific promoter, optionally wherein the cardiac or cardiomyocte-specific promoter is selected from a cTNT, α-MHC or MLC2v promoter.

9. The vector according to claim 7, wherein the promoter is a skeletal muscle or striated muscle cell-specific promoter, optionally wherein the skeletal muscle or striated muscle cell-specific promoter is selected from a MCK, MHCK7 or desmin promoter.

10. Use of the nucleic acid according to any one of claims 1 to 3, or the vector according to any one of claims 4 to 9, in the manufacture of a medicament for use in a method of treating or preventing a laminopathy.

11. The use according to claim 10, wherein the laminopathy is characterised by one or more of myopathy, cardiomyopathy, dilated cardiomyopathy, muscular dystrophy, cardiac muscular dystrophy, skeletal muscular dystrophy, progeria, neuropathy, lipoatrophy, skeletal dysplasia, lipodystrophy, leukodystrophy or dermopathy.

12. The use according to claim 10 or claim 11, wherein the laminopathy is associated with mutation to *LMNA*.

13. The use according to any one of claims 10 to 12, wherein the laminopathy is selected from: Hutchinson-Gilford Progeria Syndrome; Dilated Cardiomyopathy; Muscular Dystrophy, Congenital, Lmna-Related; Emery-Dreifuss Muscular Dystrophy 2, Autosomal Dominant; Muscular Dystrophy; Mandibuloacral Dysplasia with Type a Lipodystrophy; Cardiomyopathy, Dilated, 1a; Charcot-Marie-Tooth Disease; Limb-Girdle Muscular Dystrophy; Cardiomyopathy, Dilated, with Hypergonadotropic Hypogonadism; Emery-Dreifuss Muscular Dystrophy 3, Autosomal Recessive; Lipodystrophy, Familial Partial, Type 2; Emery-Dreifuss Muscular Dystrophy; Charcot-Marie-Tooth Disease, Axonal, Type 2b1; Heart-Hand Syndrome, Slovenian Type; Aging; Familial Partial Lipodystrophy; Restrictive Dermopathy, Lethal; Arrhythmogenic Right Ventricular Cardiomyopathy; Tooth Disease; Heart Disease; Werner Syndrome; Hypertrophic Cardiomyopathy; Left Ventricular Noncompaction; Atrioventricular Block; Calcinosis; Acroosteolysis; Autosomal Dominant Limb-Girdle Muscular Dystrophy; Diabetes Mellitus, Noninsulin-Dependent; Osteoporosis; Atrial Fibrillation; Atrial Standstill 1; Acanthosis Nigricans; Cardiac Conduction Defect; Catecholaminergic Polymorphic Ventricular Tachycardia; Mandibular Hypoplasia, Deafness, Progeroid Features, and Lipodystrophy Syndrome; Sick Sinus Syndrome; Pelger-Huet Anomaly; Charcot-Marie-Tooth Disease, Axonal, Type 2e; Congenital Generalized Lipodystrophy; Restrictive Cardiomyopathy; Congenital Fiber-Type Disproportion; Lipodystrophy, Congenital Generalized, Type 1; Myofibrillar Myopathy; Lipodystrophy, Familial Partial, Type 1; Axonal Neuropathy; Atypical Werner Syndrome; Ovarian Cystadenoma; Fanconi Anemia, Complementation Group a; Body Mass Index Quantitative Trait Locus 11; Skin Disease; Rigid Spine Muscular Dystrophy 1; Neuromuscular Disease; Hallermann-Streiff Syndrome; Bethlem Myopathy 1; Acquired Generalized Lipodystrophy; Cardiomyopathy, Dilated, 1e; Lipodystrophy, Congenital Generalized, Type 4; Undifferentiated Pleomorphic Sarcoma; Lipodystrophy, Familial Partial, Type 3; Muscular Dystrophy, Congenital Merosin-Deficient, 1a; Proximal Spinal Muscular Atrophy; Muscular Dystrophy-Dystroglycanopathy , Type B, 5; Muscular Dystrophy, Congenital, 1b; Reynolds Syndrome; Wiedemann-Rautenstrauch Syndrome; Emery-Dreifuss Muscular Dystrophy 1, X-Linked; Lipodystrophy, Congenital Generalized, Type 2; Monogenic Diabetes; Cardiomyopathy, Dilated, 1d; Myopathy, Proximal, and Ophthalmoplegia; Muscle Tissue Disease; Lipodystrophy, Familial Partial, Type 4; Cardiomyopathy, Dilated, 1h; Second-Degree Atrioventricular Block; Median Neuropathy; Intrinsic Cardiomyopathy; Prolapse of Female Genital Organ; Complete Generalized Lipodystrophy; Rigid Spine Muscular Dystrophy; Emerinopathy; Ulnar Nerve Lesion; Limb-Girdle Muscular Dystrophy Type 1b; Lmna-Related Dilated Cardiomyopathy; Pelvic Muscle Wasting; Generalized Lipodystrophy-Associated Progeroid Syndrome; Muscular Disease; Cardiomyopathy, Dilated, 1b; Autosomal Genetic Disease; Familial Isolated Arrhythmogenic Ventricular Dysplasia, Right Dominant Form; Familial Isolated Arrhythmogenic Ventricular Dysplasia, Biventricular

Form; Familial Isolated Arrhythmogenic Ventricular Dysplasia, Left Dominant Form; Lmna-Related Cardiocutaneous Progeria Syndrome; and Autosomal Semi-Dominant Severe Lipodystrophic Laminopathy.

14. Use of the nucleic acid according to any one of claims 1 to 3, or the vector according to any one of claims 4 to 9, in the manufacture of a medicament for use in a method of treating or preventing a disease characterised by hyperlipidemia.

15. The use according to claim 14, wherein the disease characterised by hyperlipidemia is selected from atherosclerosis, cardiovascular disease, stroke and a familial hyperlipidemia.