Claims

1. A recombinant agrin protein or a fragment thereof, wherein the fragment thereof comprises at least a N-terminal agrin domain (NtA domain), the laminin globular domain 2 (LG2 domain), the laminin globular domain 3 (LG3 domain) and the amino acid sequence connecting the EGF-like domain 4 (EG4 domain) and the LG3 domain of the recombinant agrin protein, and wherein at least one amino acid residue of the amino acid sequence connecting the EG4 domain and the LG3 domain of the recombinant agrin protein or the fragment thereof is modified, wherein the amino acid sequence connecting the EG4 domain and the LG3 domain of the recombinant agrin protein comprises the amino acid sequence KGLVEASAGD as shown in SEQ ID NO:65.
2. The recombinant agrin protein or a fragment thereof of claim 1, wherein the at least one modified amino acid residue of the amino acid sequence connecting the EG4 domain and the LG3 domain of the recombinant agrin protein or the fragment thereof is the A between E and S of the amino acid sequence KGLVEASAGD as shown in SEQ ID NO:65.
3. The recombinant agrin protein or a fragment thereof of any one of claims 1-2, wherein the fragment of the recombinant agrin protein further comprises the following polypeptides: a signal sequence (SS), a follistatin-like domain (FS domain), three EGF-like domains (EG domains) and one laminin globular domain (LG domain).
4. The recombinant agrin protein or a fragment thereof of any one of claims 1-2, wherein the fragment of the recombinant agrin protein comprises the following polypeptides: a signal sequence (SS), a N-terminal agrin domain (NtA domain), a follistatin-like domain (FS domain), EGF-like domain 1 (EG1 domain), laminin

globular domain 1 (LG1 domain), EGF-like domain 2 (EG2 domain), EGF-like domain 3 (EG3 domain), laminin globular domain 2 (LG2 domain), EGF-like domain 4 (EG4 domain), the amino acid sequence connecting the EGF-like domain 4 (EG4 domain) and the LG3 domain and laminin globular domain 3 (LG3 domain), wherein at least one amino acid residue of the amino acid sequence connecting the EG4 domain and the LG3 domain of the fragment is modified, wherein the amino acid sequence connecting the EG4 domain and the LG3 domain of the recombinant agrin protein comprises the amino acid sequence KGLVEASAGD as shown in SEQ ID NO:65.

5. The agrin protein or a fragment thereof of any one of claims 1-4, comprising the sequence as shown in SEQ ID NO:11.

6. A nucleic acid sequence encoding an agrin protein or a fragment thereof of any one of claims 1-5.

7. The nucleic acid sequence according to claim 6, further comprising a muscle specific promoter operably linked to the nucleic acid sequence encoding an agrin protein or a fragment thereof.

8. A vector comprising the nucleic acid sequence according to claim 6 or claim 7.

9. A recombinant chimeric laminin-nidogen protein or a fragment thereof comprising the sequence as shown in SEQ ID NO: 39 or comprising the sequence as shown in SEQ ID NO: 68.

10. A nucleic acid sequence encoding a protein according to claim 9.

11. The nucleic acid sequence according to claim 10, further comprising a muscle specific promoter or a ubiquitous promoter operably linked to the nucleic acid sequence encoding a protein according to claim 9.

12. A vector comprising the nucleic acid sequence according to claim 10 or claim 11.

13. A composition comprising the agrin protein or a fragment thereof of any one of claims 1-5 and a recombinant chimeric laminin-nidogen protein or a fragment thereof comprising at least the LN domain of laminin and the G3 domain of nidogen or comprising at least the LN domain of laminin and the G2 and G3 domain of nidogen, preferably an alpha LNNd protein, more preferably the recombinant chimeric laminin-nidogen protein or a fragment thereof according to claim 9, or the nucleic acid sequence of claim 6 or 7 and the nucleic acid sequence of claim 10 or 11, or the vector of claim 8 and the vector of claim 12, or a vector comprising the nucleic acid sequence of claim 6 or 7 and the nucleic acid sequence of claim 10 or 11, preferably an AAV vector comprising the nucleic acid sequence of claim 6 or 7 and the nucleic acid sequence of claim 10 or 11.

14. The agrin protein or a fragment thereof of any one of claims 1-5 and/or the recombinant chimeric laminin-nidogen protein or a fragment thereof of claim 9, or the nucleic acid sequence of claim 6 or 7 and/or the nucleic acid sequence of claim 10 or 11, or the vector of claim 8 and/or the vector of claim 12, or the vector comprising the nucleic acid sequence of claim 6 or 7 and the nucleic acid sequence of claim 10 or 11, and/or the composition of claim 13 for use in the prophylaxis and/or treatment of congenital muscular dystrophies.

15. The proteins, nucleic acid sequences, vectors or the composition for use according to claim 14, wherein the congenital muscular dystrophy is (laminin-α2) LAMA2-related muscular dystrophy.

16. The proteins, nucleic acid sequences, vectors or the composition for use according to claim 14 or 15 wherein an AAV vector for expression of the recombinant laminin-nidogen protein and an AAV vector for expression of the agrin protein or a fragment thereof are used in combination with immunosuppressants or omigapil

(N-(dibenz(b,f)oxepin-10-ylmethyl)-N-methyl-N-prop-2-ynylamine).

17. Use of the agrin protein or a fragment thereof of any one of claims 1-5 and/or the recombinant chimeric laminin-nidogen protein or a fragment thereof of claim 9, or the nucleic acid sequence of claim 6 or 7 and/or the nucleic acid sequence of claim 10 or 11, or the vector of claim 8 and/or the vector of claim 12, or the vector comprising the nucleic acid sequence of claim 6 or 7 and the nucleic acid sequence of claim 10 or 11, and/or the composition of claim 13 in the manufacture of a medicament for the prophylaxis and/or treatment of congenital muscular dystrophies.

18. The use of claim 17 wherein the congenital muscular dystrophy is (laminin-α2) LAMA2-related muscular dystrophy.

19. The use of claim 17 or 18 wherein an AAV vector for expression of the recombinant laminin-nidogen protein and an AAV vector for expression of the agrin protein or a fragment thereof are used in combination with immunosuppressants or omigapil (N-(dibenz(b,f)oxepin-10-ylmethyl)-N-methyl-N-prop-2-ynylamine).