significant therapeutic effects (vs untreated) at said suboptimal dose (Figure 10B and 11B). Moreover, the observed difference in activity between the full length ATP7B and T2 constructs at a dose of 1×10^{10} vg / mouse was also shown to be statistically significant for these two therapeutic effects (Fig. 12 and Fig.14).

These observations indicated that both a nucleic acid construct encoding the truncated form ATP7B(d57-486) and vectors that carry it, in particular AAV vectors, enable to overcome the most relevant pathological effects of an accumulation of copper linked to a deficiency or dysfunction of ATP7B and thus can be very suitable for gene therapy applied to a condition caused by a deficiency or dysfunction of Copper-transporting ATPase 2, such as Wilson's disease, or a disease and/or condition associated with a decrease of ATP7B-dependent lysosomal exocytosis and copper accumulation. Moreover, unexpectedly the truncated form ATP7B(d57-486) and vectors that carry it, were shown to achieve normalization of some of these pathological manifestations of the disease at dosages where the full length ATP7B protein and vectors encoding the same proved to be less effective.

Therefore, in a first aspect the invention relates to a nucleic acid construct (hereinafter also referred as "nucleic acid construct of the invention"), that comprises: a) a nucleotide sequence of an eukaryotic promoter; b) a nucleotide sequence encoding a truncated Copper-transporting ATPase 2 (ATP7B) in which the N-terminal heavy metal associated sites HMA 1, HMA 2, HMA 3, and HMA 4 are totally deleted and HMA 5 and HMA 6 remain undeleted; c) a polyadenylation signal sequence; and d) 5' Terminal Repeat and 3'Terminal Repeat sequences of a virus.

In another aspect, the invention relates to a viral expression vector (hereinafter also referred as "expression vector of the invention"), that comprises a nucleic acid construct of the invention.

In another aspect, the invention relates to a host cell comprising a nucleic acid construct or a viral expression vector of the invention.

In another aspect, the invention relates to a viral particle (hereinafter also referred as "viral particle of the invention"), that comprises a nucleic construct or a viral expression vector of the invention. Preferably, the nucleic acid construct constitutes the genomic sequence of the viral vector.

In another aspect, the invention relates to a pharmaceutical composition that comprises a product of the invention, i.e. a product that comprises a nucleic acid construct of the invention, and a pharmaceutically acceptable carrier. The term "product of the invention" as used herein refers to and indistinctively covers any of: a) the nucleic acid construct of the invention; b) the

CLAIMS

1. A nucleic acid construct that comprises

a) a nucleotide sequence of an eukaryotic promoter;

b) a nucleotide sequence encoding a truncated Copper-transporting ATPase 2 in which the N-terminal Heavy-Metal-Associated sites HMA 1, HMA 2, HMA 3, and HMA 4 are totally deleted and HMA 5 and HMA 6 remain undeleted;

c) a polyadenylation signal sequence; and,

d) 5' Terminal Repeat and 3'Terminal Repeat sequences of a virus.

2. The nucleic acid construct according to claim 1, wherein the deletion in the truncated ATP7B comprises amino acids 57 to 486 of the SEQ.ID.NO.2 sequence.

3. The nucleic acid construct according to any of claims 1 or 2, wherein the amino acid sequence of truncated Copper-transporting ATPase2 is SEQ.ID.NO.7.

4. The nucleic acid construct according to claim 3, wherein the nucleotide sequence encoding the truncated Copper-transporting ATPase 2 is selected from the group consisting of

a) the coding sequence CDS of SEQ.ID.NO.6, bases 473..3580;

b) the sequence SEQ.ID.NO.8; and

c) a sequence wherein at least 827, at least 879, at least 931, or at least 983 of the codons encoding truncated Copper-transporting ATPase 2 are identical to the codons of coding sequence SEQ.ID.NO.8.

5. The nucleic acid construct according to any of claims 1 – 4, wherein the nucleotide sequence of the eukaryotic promoter is a nucleotide sequence of the α1-antitrypsin gene promoter, or a chimeric promoter sequence that comprises an α1-antitrypsin gene promoter sequence combined with an albumin gene enhancer element.

6. The nucleic acid construct according to any of claims 1 – 5, wherein the nucleotide sequence of the eukaryotic promoter is the sequence delimited by bases 156..460 of SEQ.ID.NO.1 (AAT), or SEQ.ID.NO.5 (EalbPa1AT).

7. The nucleic acid construct according to claim 1, wherein the 5'ITR and 3'ITR sequences are of an adeno-associated virus (AAV).

8. The nucleic acid construct according to claim 7, wherein the 5'ITR and 3'ITR sequences of an AAV are of a serotype selected from the group consisting of AAV1, AAV2, and AAV4, preferably are of the AAV2 serotype.

9. A viral expression vector that comprises a nucleic acid construct according to any of claims 1 – 8.

10. The viral expression vector according to claim 9, wherein the vector is an AAV vector.

11. A host cell comprising a nucleic acid construct according to any of claims 1–8, or a viral expression vector according to Claim 9.

12. A viral particle that comprises a nucleic acid construct according to any of claims 1 – 8 or a viral expression vector according to claim 9.

13. The viral particle according to claim 12, wherein the viral particle comprises capsid proteins of an AAV.

14. The viral particle according to claim 13, wherein the viral particle comprises capsid proteins of an AAV of a serotype selected from the group consisting of AAV1, AAV5, AAV7, AAV8, AAV9 and AAV10, preferably from the AAV8 or AAV9 serotype.

15. The viral particle according to claim 14, wherein the 5'ITR and 3'ITR sequences of the nucleic acid construct are of an AAV2 serotype and the capsid proteins are of an AAV8 serotype.

16. A pharmaceutical composition that comprises a nucleic acid construct according to any of claims 1–8, an expression vector according to claim 9-10, a host cell according to claim 11 or a viral particle according to any of claims 12-15, and a pharmaceutically acceptable carrier.

17. A kit comprising a nucleic acid construct according to any of claims 1–8, an expression vector according to claims 9-10, a host cell according to claim 11 or a viral particle according to any of claims 12-15 or a pharmaceutical composition according to claim 16 in one or more containers, optionally further comprising instructions or packaging materials that describe how to administer the nucleic acid construct, vector, host cell, viral particle or pharmaceutical composition to a patient.

18. A nucleic acid construct according to any of claims 1–8, an expression vector according to claims 9-10, a host cell according to claim 11 or a viral particle according to any of claims 12-15, for use as a medicament.

19. A nucleic acid construct according to any of claims 1–8, an expression vector according to claims 9-10, a host cell according to claim 11 or a viral particle according to any of claims 12-15 or a pharmaceutical composition according to claim 16, for use in the treatment of a condition caused by a deficiency or dysfunction of Copper-transporting ATPase 2, preferably in the treatment of Wilson's disease.

20. Use of a nucleic acid construct according to any of claims 1–8, an expression vector according to claims 9-10, a host cell according to claim 11, a viral particle according to any of claims 12-15 or a pharmaceutical composition according to claim 16 in the preparation of a medicament for the treatment of a condition caused by a deficiency or dysfunction of Copper-transporting ATPase 2, preferably in the treatment of Wilson's disease.

21. A process of producing viral particles according to any of claims 12-15, comprising the steps of:

a) culturing a host cell according to claim 11 in a culture medium; and

b) harvesting the viral particles from the cell culture supernatant and/or inside the cells.

22. Use of the nucleic acid construct of any of claims 1-8 or the viral expression vector of claims 9-10 for the production of viral particles.