CLAIMS

1. Use of an autologous genetically modified cells in the manufacture of a medicament for the treatment of a type VII collagen (C7) deficiency in a patient suffering from the deficiency, wherein the cells, having been obtained from the dermis or epidermis of the C7-deficient patient, have been contacted with a transducing lentiviral vector comprising a nucleotide sequence encoding COL7A1 or a functional variant thereof to form the autologous genetically modified cells having a vector copy number wherein said lentiviral vector has a transducing vector copy number in the range of 0.1 to 5.0 copies per cell; and the said autologous genetically modified cells have been cultured; wherein an effective amount of the genetically modified cells is to be administered to the C7-deficient patient, and wherein the transducing lentiviral vector further comprises (a) a modified 5' long terminal repeat (LTR), wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) at least one lentiviral central polypurine tract element, and (c) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted.

2. The use of claim 1, wherein the cells are selected from fibroblasts and keratinocytes.

3. The use of claim 1, wherein the C7-deficiency is dystrophic epidermolysis bullosa.

4. The use of claim 1, wherein the C7-deficiency is a dystrophic epidermolysis bullosa, recessive dystrophic epidermolysis bullosa (RDEB), dominant dystrophic epidermolysis bullosa (DDEB), Hallopeau-Siemens, non-Hallopeau-Siemens RDEB, RDEB inversa, pretibial RDEB, acral RDEB, or RDEB centripetalis.

5. The use of claim 1, wherein said transducing lentiviral vector is in the form of a lentiviral vector particle.

6. The use of claim 1 or claim 2, wherein the genetically modified cells are to be administered to the patient by injection, topically, orally, or embedded in a biocompatible matrix.

7. An autologous genetically modified fibroblast from a patient suffering from a Type VII collagen deficiency transduced with a lentiviral vector particle comprising a functional *COL7A1* gene or a functional variant thereof, and expressing type VII collagen, wherein said lentiviral vector particle has a transducing vector copy number in the range of 0.1 to 5.0 copies per cell, wherein said transducing lentiviral vector particle is constructed from a transfer lentiviral vector comprising (a) a modified 5' long terminal repeat in LTR, wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) a functional *COL7A1* gene, (c) at least one lentiviral central polypurine tract, and (d) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted, wherein the *COL7A1* gene or the functional variant thereof is incorporated into the cells to form genetically modified cells having a functional *COL7A1* gene.

8. A self-inactivating lentiviral vector formed from a transfer vector comprising (a) a modified 5' long terminal in LTR, wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) the *COL7A1* gene or a functional variant thereof, (c) at least one lentiviral central polypurine tract element, and (d) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, and, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted, wherein the deleted PRE is a woodchuck post-transcriptional regulatory element PRE (WPRE).

9. A transfer vector comprising the amino acid sequence set forth in SEQ ID NO: 34.

10. A lentiviral vector particle comprising the self-inactivating lentiviral vector of claim 8 or the transfer vector of claim 9.

11. A lentiviral vector particle constructed from a lentiviral expression plasmid comprising (a) a modified 5' long terminal repeat in LTR, wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) a functional *COL7A1* gene, (c) at least one lentiviral central polypurine tract, and (d) a modified 3' LTR, wherein the modified 3'

LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted.

12. A stable virus packaging cell line producing the lentiviral vector particle of claim 10 or claim 11.

13. A pharmaceutical composition comprising a fibroblast obtained from a patient suffering from RDEB or DDEB transduced with the lentiviral vector of claim 10 or claim 11.

14. A cell transduced *in vitro* or *ex vivo* with the vector of claim 10 or claim 11.

15. An autologous population of cells for use in treating a patient suffering from pseudosyndactyly, wherein said autologous population of cells is to be obtained from said patient and transduced with a lentiviral vector particle comprising a functional *COL7A1* gene or a functional variant thereof, and expressing type VII collagen, wherein said lentiviral vector particle has a transducing vector copy number in the range of 0.1 to 5.0 copies per cell, wherein said transducing lentiviral vector particle is constructed from a transfer lentiviral vector comprising (a) a modified 5' long terminal repeat in LTR, wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) a functional *COL7A1* gene, (c) at least one lentiviral central polypurine tract, and (d) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted, wherein the *COL7A1* gene or the functional variant thereof is incorporated into the cells to form genetically modified cells having a functional *COL7A1* gene.

16. A method of making an isolated population of Type VII collagen (C7) expressing genetically modified cells autologous to a patient suffering from C7 deficiency comprising: contacting cells, obtained from the dermis or epidermis of the C7-deficient patient, with a transducing lentiviral vector particle comprising the *COL7A1* gene or a functional variant thereof to form autologous genetically modified cells comprising the *COL7A1* gene having a vector copy number of wherein said lentiviral vector particle has a transducing vector copy number in the range of 0.1 to 5.0 copies per cell, and culturing said autologous genetically modified cells to obtain an isolated population of

C7 expressing genetically modified cells, wherein said transducing lentiviral vector particle is constructed from a transfer lentiviral vector comprising (a) a modified 5' long terminal repeat in LTR, wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) a functional *COL7A1* gene, (c) at least one lentiviral central polypurine tract, and (d) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted, wherein the *COL7A1* gene or the functional variant thereof is incorporated into the cells to form genetically modified cells having a functional *COL7A1* gene.

17. An isolated population of Type VII collagen (C7)-expressing genetically modified cells produced by the method of claim 16.

18. A pharmaceutical formulation comprising the isolated population of claim 17.

19. A method of increasing the integrated transgene copy number per cell in genetically modified human dermal fibroblasts or keratinocytes comprising
    (a) contacting a transducing lentiviral vector comprising a nucleotide sequence encoding a *COL7A1* gene or a functional variant thereof with a human dermal fibroblast or keratinocyte obtained from a C7-deficient patient to form a first transduction composition;
    (b) subjecting said first transduction composition to spinoculation to form transduced human dermal fibroblast or keratinocyte;
    (c) contacting the transduced human dermal fibroblasts or keratinocytes of step (b) with a second transducing lentiviral vector to form a second transduction composition; and
    (d) subjecting said first transduction composition to spinoculation to form transduced human dermal fibroblast or keratinocyte,

    wherein the integrated transgene copy number of the transduced human dermal fibroblasts or keratinocytes is at least 5, 10, 15, 20, 25, 27, 28, 29, 30, 35, 40, 45, or 50- fold higher relative to transduced human dermal fibroblasts or keratinocytes not subjected to spinoculation or a second transduction step, and wherein the transducing lentiviral vector further comprises (a) a modified 5' long terminal repeat (LTR), wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) at least one

lentiviral central polypurine tract element, and (c) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post- transcriptional regulatory element (PRE) has been deleted.

20. Autologous genetically modified cells for use in a method for treating a patient suffering from a type VII collagen (C7) deficiency, wherein said method comprises:

(i) contacting cells, obtained from the dermis or epidermis of the C7-deficient patient, with a transducing lentiviral vector comprising a nucleotide sequence encoding COL7A1 or a functional variant thereof to form the autologous genetically modified cells having a vector copy number wherein said lentiviral vector has a transducing vector copy number in the range of 0.1 to 5.0 copies per cell; and

(ii) culturing said autologous genetically modified cells,

wherein an effective amount of the genetically modified cells to the C7-deficient patient are to be administered to the patient, and wherein the transducing lentiviral vector further comprises (a) a modified 5' long terminal repeat (LTR), wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) at least one lentiviral central polypurine tract element, and (c) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted.

21. Use of an autologous population of cells in the manufacture of a medicament for the treatment of a patient suffering from pseudosyndactyly, wherein said autologous population of cells is to be obtained from said patient and transduced with a lentiviral vector particle comprising a functional *COL7A1* gene or a functional variant thereof, and expressing type VII collagen, wherein said lentiviral vector particle has a transducing vector copy number in the range of 0.1 to 5.0 copies per cell, wherein said transducing lentiviral vector particle is constructed from a transfer lentiviral vector comprising (a) a modified 5' long terminal repeat in LTR, wherein the promoter of the modified 5' LTR is a cytomegalovirus promoter, (b) a functional *COL7A1* gene, (c) at least one lentiviral central polypurine tract, and (d) a modified 3' LTR, wherein the modified 3' LTR comprises a deletion relative to the wild-type 3' LTR, wherein a hepatitis virus post-transcriptional regulatory element (PRE) has been deleted, wherein the *COL7A1* gene or the functional variant thereof is

incorporated into the cells to form genetically modified cells having a functional *COL7A1* gene.