comprising one or more polynucleotides encoding a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, a Keratin type I cytoskeletal 17 polypeptide and/or a chimeric polypeptide thereof.

[0011] Disclosed is a pharmaceutical composition comprising a virus comprising a vector, wherein the vector comprises one or more transgenes encoding a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, or a chimeric polypeptide thereof, and a pharmaceutically acceptable carrier. In some examples, the virus is an adenovirus, adeno-associated virus, retrovirus, lentivirus, sendai virus, herpes simplex virus, vaccinia virus, or any hybrid virus thereof. In some examples, the virus is replication-defective. In some examples, the virus is a herpes simplex virus (HSV). In some examples, the herpes simplex virus is a herpes simplex type 1 virus, a herpes simplex type 2 virus, or any derivatives thereof. In some examples, the herpes simplex virus comprises a modified envelope. In some examples, the modified envelope alters the herpes simplex virus tissue tropism relative to a wild-type herpes simplex virus. In some examples, the modified envelope comprises a mutant herpes simplex virus glycoprotein. In some examples, the vector is an HSV-1 amplicon or an HSV-1 hybrid amplicon. In some examples, the HSV-1 hybrid amplicon is an HSV/AAV hybrid amplicon, an HSV/EBV hybrid amplicon, and HSV/EBV/RV hybrid amplicon, or an HSV/*Sleeping Beauty* hybrid amplicon. In some examples, the vector is a recombinant herpes simplex virus genome. In some examples, the recombinant herpes simplex virus genome is a recombinant HSV-1 genome, a recombinant HSV-2 genome, or any derivatives thereof. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in an immediate early herpes simplex virus gene. In some examples, the herpes simplex virus gene is ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, or UL55. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP27, and UL55 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP22, ICP27, ICP47, and UL55 genes. In some examples, the inactivating mutation in the ICP4, ICP27, and UL55 genes is a deletion of the coding sequence of the ICP4, ICP27, and UL55 genes. In some examples, the inactivating mutation in the ICP22 and ICP47 genes is a deletion in the promoter region of the ICP22 and ICP47 genes. In some

examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4 and ICP22 genes. In some example, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0 and ICP4 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, and ICP22 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, and ICP27 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, ICP27, and UL55 genes. In some examples, the inactivating mutation is a deletion of the coding sequence of the genes. In some examples, the recombinant herpes simplex virus genome further comprises an inactivating mutation in the ICP47 gene, an inactivating mutation in the UL41 gene, or an inactivation mutation in the ICP47 and UL41 genes. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more of the ICP4 viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within the UL41 viral gene locus. In some examples, the vector is capable of replicating within a target cell when delivered into said target cell. In some examples, the pharmaceutically acceptable carrier is suitable for topical or transdermal administration. In some examples, the one or more transgenes comprises an miRNA binding site. In some examples, the one or more transgenes are operably linked to one or more heterologous promoters. In some examples, the one or more heterologous promoters are one or more of the human cytomegalovirus (HCMV) immediate early promoter, the elongation factor-1 (EF1) promoter, and/or any combinations thereof. In some example, the vector comprises a transgene encoding a Collagen alpha-1 (VII) chain polypeptide. In some examples, the vector comprises two transgenes, wherein each transgene encodes a Collagen alpha-1 (VII) chain polypeptide. In some examples, the Collagen alpha-1 (VII) chain polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 2. In some examples, the collagen alpha-1 (VII) chain polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 2. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements anchoring fibril

formation of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements epithelial basement membrane organization and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements the formation of hydroxylysine residues on one or more collagen polypeptides of a subject when the Lysyl hydroxylase 3 polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the vector comprises at least a first transgene and a second transgene. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide and the second transgene encodes a Lysyl hydroxylase 3 polypeptide. In some examples, the vector comprises a transgene that is polycistronic. In some examples, the polycistronic transgene encodes a Collagen alpha-1 (VII) chain polypeptide on a first open reading frame (ORF) and a Lysyl hydroxylase 3 polypeptide on a second open reading frame (ORF). In some examples, the first and second ORFs are separated by an internal ribosomal entry site (IRES). In some examples, the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide are at about an equimolar ratio when the polypeptides are expressed in one or more target cells of a subject. In some examples, the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide enhance, increase, augment, and/or supplement anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptides are expressed in one or more target cells of the subject. In some examples, the chimeric polypeptide comprises a linker polypeptide between the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide. In some examples, the linker polypeptide is a T2A, P2A, E2A, or F2A linker polypeptide. In some

examples, the linker polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12. In some examples, the chimeric polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26 or SEQ ID NO: 28. In some examples, the chimeric polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject.

[0011a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising: a) a replication-defective herpes simplex virus (HSV) comprising a recombinant herpes simplex virus genome, wherein the recombinant herpes simplex virus genome comprises one or more transgenes encoding a polypeptide selected from the group consisting of a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, and a Keratin type I cytoskeletal 17 polypeptide; and b) a pharmaceutically acceptable carrier.

[0011b] In another aspect, the present disclosure refers to a pharmaceutical composition useful for delivery of one or more transgenes to the skin of a subject, comprising: a) a replication-defective herpes simplex virus (HSV) comprising a recombinant herpes simplex virus genome, wherein the recombinant herpes simplex virus genome comprises one or more polynucleotides encoding the one or more transgenes; and b) a pharmaceutically acceptable carrier; wherein the pharmaceutical composition is a topical, transdermal, subcutaneous, or intradermal composition; and wherein the replication-defective HSV is suitable for delivering the one or more polynucleotides encoding the one or more transgenes to one or more target cells of the epidermis and/or dermis of the subject.

[0012] Disclosed is a method of providing prophylactic, palliative, or therapeutic relief of a wound, disorder, or disease of the skin in a subject, the method comprising topically or transdermally administering a pharmaceutical composition capable of enhancing, increasing, augmenting, and/or supplementing the levels of a Collagen alpha-1 (VII) chain polypeptide and/or a Lysyl hydroxylase 3 polypeptide in one or more cells of the subject. In some examples, the pharmaceutical composition comprises a virus comprising a vector, wherein the vector comprises one or more transgenes encoding a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, or a chimeric polypeptide thereof, and a pharmaceutically acceptable carrier. In some examples, the virus is an adenovirus, adeno-associated virus, retrovirus, lentivirus, sendai virus, herpes simplex virus, vaccinia virus, or any hybrid virus thereof. In some examples, the virus is replication-defective. In some examples, the virus is a herpes simplex virus (HSV). In some examples, the herpes simplex virus is a herpes simplex type 1 virus, a herpes simplex type 2 virus, or any derivatives thereof. In some examples, the herpes simplex virus comprises a modified envelope. In some examples, the modified envelope alters the herpes simplex virus tissue tropism relative to a wild-type herpes simplex virus. In some examples, the modified envelope comprises a mutant herpes simplex virus glycoprotein. In some examples, the vector is an HSV-1 amplicon or an HSV-1 hybrid amplicon. In some examples, the HSV-1 hybrid amplicon is an HSV/AAV hybrid amplicon, an HSV/EBV hybrid amplicon, and HSV/EBV/RV hybrid amplicon, or an HSV/*Sleeping Beauty* hybrid amplicon. In some examples, the vector is a recombinant herpes simplex virus genome. In some examples, the recombinant herpes simplex virus genome is a recombinant HSV-1 genome, a recombinant HSV-2 genome, or any derivatives thereof. In

some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in an immediate early herpes simplex virus gene. In some examples, the herpes simplex virus gene is ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, or UL55. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP27, and UL55 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP22, ICP27, ICP47, and UL55 genes. In some examples, the inactivating mutation in the ICP4, ICP27, and UL55 genes is a deletion of the coding sequence of the ICP4, ICP27, and UL55 genes. In some examples, the inactivating mutation in the ICP22 and ICP47 genes is a deletion in the promoter region of the ICP22 and ICP47 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4 and ICP22 genes. In some example, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0 and ICP4 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, and ICP22 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, and ICP27 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, ICP27, and UL55 genes. In some examples, the inactivating mutation is a deletion of the coding sequence of the genes. In some examples, the recombinant herpes simplex virus genome further comprises an inactivating mutation in the ICP47 gene, an inactivating mutation in the UL41 gene, or an inactivation mutation in the ICP47 and UL41 genes. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more of the ICP4 viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within the UL41 viral gene locus. In some examples, the vector is capable of replicating within a target cell when delivered into said target cell. In some examples, the pharmaceutically acceptable carrier is suitable for topical or transdermal administration. In some examples, the one or more transgenes comprises an miRNA binding site. In some examples, the one or more transgenes are operably linked to one or more heterologous promoters. In some examples, the one or

more heterologous promoters are one or more of the human cytomegalovirus (HCMV) immediate early promoter, the elongation factor-1 (EF1) promoter, and/or any combinations thereof. In some examples, the vector comprises a transgene encoding a Collagen alpha-1 (VII) chain polypeptide. In some examples, the vector comprises two transgenes, wherein each transgene encodes a Collagen alpha-1 (VII) chain polypeptide. In some examples, the Collagen alpha-1 (VII) chain polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 2. In some examples, the collagen alpha-1 (VII) chain polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 2. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements epithelial basement membrane organization and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements the formation of hydroxylysine residues on one or more collagen polypeptides of a subject when the Lysyl hydroxylase 3 polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the vector comprises at least a first transgene and a second transgene. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide and the second transgene encodes a Lysyl hydroxylase 3 polypeptide. In some examples, the vector comprises a transgene that is polycistronic. In some examples, the polycistronic transgene encodes a Collagen alpha-1 (VII) chain polypeptide on a first open reading frame (ORF) and a Lysyl hydroxylase 3 polypeptide on a second open reading frame (ORF). In some examples, the first and second ORFs are separated by an internal

ribosomal entry site (IRES). In some examples, the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide are at about an equimolar ratio when the polypeptides are expressed in one or more target cells of a subject. In some examples, the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide enhance, increase, augment, and/or supplement anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptides are expressed in one or more target cells of the subject. In some examples, the chimeric polypeptide comprises a linker polypeptide between the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide. In some examples, the linker polypeptide is a T2A, P2A, E2A, or F2A linker polypeptide. In some examples, the linker polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12. In some examples, the chimeric polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26 or SEQ ID NO: 28. In some examples, the chimeric polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the pharmaceutical composition is administered one, two three, four, five or more times per day. In some examples, the pharmaceutical composition is administered to one or more affected and/or unaffected areas of the subject. In some examples, the disease or disorder of the skin is one or more of epidermolysis bullosa, skin cancer, psoriasis, lichen planus, lupus, rosacea, eczema, cutaneous candidiasis, cellulitis, impetigo, decubitus ulcers, erysipelas, ichthyosis vulgaris, dermatomyositis, acrodermatitis, stasis dermatitis, nethertons syndrome, epidermolysis bullosa simplex (LAMB3 gene), autosomal recessive congenital ichthyosis, xeroderma pigmentosa, and pemphigoid.

[0013] Disclosed is an isolated chimeric polypeptide, wherein the isolated chimeric polypeptide comprises a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, and a linker polypeptide, wherein the Collagen alpha-1 (VII) chain polypeptide and the Lysyl hydroxylase 3 polypeptide are separated by the linker polypeptide, to polynucleotides encoding the same, to vectors

comprising the polynucleotides, and to host cells comprising the vectors. In some examples, the vector is an HSV-1 amplicon or an HSV-1 hybrid amplicon. In some examples, the HSV-1 hybrid amplicon is an HSV/AAV hybrid amplicon, an HSV/EBV hybrid amplicon, and HSV/EBV/RV hybrid amplicon, or an HSV/*Sleeping Beauty* hybrid amplicon. In some examples, the vector is a recombinant herpes simplex virus genome. In some examples, the recombinant herpes simplex virus genome is a recombinant HSV-1 genome, a recombinant HSV-2 genome, or any derivatives thereof. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in an immediate early herpes simplex virus gene. In some examples, the herpes simplex virus gene is ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, or UL55. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP27, and UL55 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP22, ICP27, ICP47, and UL55 genes. In some examples, the inactivating mutation in the ICP4, ICP27, and UL55 genes is a deletion of the coding sequence of the ICP4, ICP27, and UL55 genes. In some examples, the inactivating mutation in the ICP22 and ICP47 genes is a deletion in the promoter region of the ICP22 and ICP47 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4 and ICP22 genes. In some example, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0 and ICP4 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, and ICP22 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, and ICP27 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, ICP27, and UL55 genes. In some examples, the inactivating mutation is a deletion of the coding sequence of the genes. In some examples, the recombinant herpes simplex virus genome further comprises an inactivating mutation in the ICP47 gene, an inactivating mutation in the UL41 gene, or an inactivation mutation in the ICP47 and UL41 genes. In some examples, the recombinant herpes simplex virus genome comprises the polynucleotide within one or more viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the polynucleotide within one or more of the ICP4

viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the polynucleotide within the UL41 viral gene locus.

[0014] Disclosed is a vector comprising one or more polynucleotides encoding a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, a Keratin type I cytoskeletal 17 polypeptide, or any combinations thereof, wherein the vector is a recombinant herpes simplex virus genome, and to host cells comprising the vector. In some examples, the recombinant herpes simplex virus genome is a recombinant HSV-1 genome, a recombinant HSV-2 genome, or any derivatives thereof. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in an immediate early herpes simplex virus gene. In some examples, the herpes simplex virus gene is ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, or UL55. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP27, and UL55 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP22, ICP27, ICP47, and UL55 genes. In some examples, the inactivating mutation in the ICP4, ICP27, and UL55 genes is a deletion of the coding sequence of the ICP4, ICP27, and UL55 genes. In some examples, the inactivating mutation in the ICP22 and ICP47 genes is a deletion in the promoter region of the ICP22 and ICP47 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4 and ICP22 genes. In some example, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0 and ICP4 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, and ICP22 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, and ICP27 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, ICP27, and UL55 genes. In some examples, the inactivating mutation is a deletion of the coding sequence of the genes. In some examples, the recombinant herpes simplex virus genome further comprises an inactivating mutation in the ICP47 gene, an inactivating mutation in the UL41 gene, or an inactivation mutation in the ICP47 and UL41 genes. In some examples, the recombinant herpes simplex virus genome comprises the one or more polynucleotides within one or more

viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more polynucleotides within one or more of the ICP4 viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more polynucleotides within the UL41 viral gene locus. In some examples, the vector comprises one polynucleotide encoding a Collagen alpha-1 (VII) chain polypeptide. In some examples, the vector comprises two polynucleotides encoding a Collagen alpha-1 (VII) chain polypeptide.

[0015] Disclosed are methods of collecting a herpes simplex virus, wherein a vector of interest is packaged within said herpes simplex virus. In some examples the method comprises the steps of contacting a host cell with a vector encoding a helper virus, contacting said host cell with a HSV-1 amplicon or HSV-1 hybrid amplicon comprising one or more polynucleotides described herein, and collecting the Herpes simplex virus generated by said host cell. In some examples, the method comprises the steps of contacting a complementing host cell with a recombinant herpes simplex virus genome vector comprising one or more polynucleotides described herein, and collecting the herpes simplex virus generated by said complementing host cell. In some examples, the collected herpes simplex virus is a herpes simplex type 1 virus, a herpes simplex type 2 virus, or any derivatives thereof.

[0016] Disclosed is a kit comprising a pharmaceutical composition described herein and instructions for administering the pharmaceutical composition.

[0017] Disclosed is a pharmaceutical composition comprising a virus comprising a vector, wherein the vector comprises one or more transgenes encoding a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, a Keratin type I cytoskeletal 17 polypeptide, or a chimeric polypeptide thereof, and a pharmaceutically acceptable carrier. In some examples, the virus is an adenovirus, adeno-associated virus, retrovirus, lentivirus, sendai virus, herpes simplex virus, vaccinia virus, or any hybrid virus thereof. In some examples, the virus is replication-defective. In some examples, the virus is a herpes simplex virus (HSV). In some examples, the herpes simplex virus is a herpes simplex type 1 virus, a herpes simplex type 2 virus, or any derivatives thereof. In some examples, the vector is an HSV-1 amplicon or an HSV-1

hybrid amplicon. In some examples, the HSV-1 hybrid amplicon is an HSV/AAV hybrid amplicon, an HSV/EBV hybrid amplicon, and HSV/EBV/RV hybrid amplicon, or an HSV/*Sleeping Beauty* hybrid amplicon. In some examples, the vector is a recombinant herpes simplex virus genome. In some examples, the recombinant herpes simplex virus genome is a recombinant HSV-1 genome, a recombinant HSV-2 genome, or any derivatives thereof. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in an immediate early herpes simplex virus gene. In some examples, the herpes simplex virus gene is ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, or UL55. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP27, and UL55 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP22, ICP27, ICP47, and UL55 genes. In some examples, the inactivating mutation in the ICP4, ICP27, and UL55 genes is a deletion of the coding sequence of the ICP4, ICP27, and UL55 genes. In some examples, the inactivating mutation in the ICP22 and ICP47 genes is a deletion in the promoter region of the ICP22 and ICP47 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4 and ICP22 genes. In some example, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0 and ICP4 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, and ICP22 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, and ICP27 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, ICP27, and UL55 genes. In some examples, the inactivating mutation is a deletion of the coding sequence of the genes. In some examples, the recombinant herpes simplex virus genome further comprises an inactivating mutation in the ICP47 gene, an inactivating mutation in the UL41 gene, or an inactivation mutation in the ICP47 and UL41 genes. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more of the ICP4 viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within

the UL41 viral gene locus. In some examples, the vector is capable of replicating within a target cell when delivered into said target cell. In some examples, the pharmaceutically acceptable carrier is suitable for topical or transdermal administration. In some examples, the pharmaceutically acceptable carrier is suitable for subcutaneous or intradermal administration. In some examples, the one or more transgenes comprises an miRNA binding site. In some example, the vector comprises a transgene encoding a Collagen alpha-1 (VII) chain polypeptide. In some example, the vector comprises a transgene encoding a Lysyl hydroxylase 3 polypeptide. In some example, the vector comprises a transgene encoding a Keratin type I cytoskeletal 17 polypeptide. In some examples, the vector comprises two transgenes, wherein each transgene encodes a Collagen alpha-1 (VII) chain polypeptide. In some examples, the Collagen alpha-1 (VII) chain polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 2. In some examples, the collagen alpha-1 (VII) chain polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 2. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements epithelial basement membrane organization and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements the formation of hydroxylysine residues on one or more collagen polypeptides of a subject when the Lysyl hydroxylase 3 polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Keratin type I cytoskeletal 17 polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 30. In some

examples, the Keratin type I cytoskeletal 17 polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 30. In some examples, the Keratin type I cytoskeletal 17 polypeptide enhances, increases, augments, and/or supplements wound healing in a subject. In some examples, the vector comprises at least a first transgene and a second transgene. In some examples, the first transgene and the second transgene each encode a Collagen alpha-1 (VII) chain polypeptide. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide and the second transgene encodes a Lysyl hydroxylase 3 polypeptide. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide and the second transgene encodes a Keratin type I cytoskeletal 17 polypeptide. In some examples, the first transgene encodes a Lysyl hydroxylase 3 polypeptide and the second transgene encodes a Keratin type I cytoskeletal 17 polypeptide. In some examples, the vector comprises at least a first transgene, a second transgene, and a third transgene. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide, the second transgene encodes a Lysyl hydroxylase 3 polypeptide, and the third transgene encodes a Keratin type I cytoskeletal 17 polypeptide.

[0018] Disclosed is a method of providing prophylactic, palliative, or therapeutic relief of a wound, disorder, or disease of the skin in a subject, the method comprising administering to the subject a pharmaceutical composition comprising a vector, wherein the vector is a recombinant herpes simplex virus genome, and wherein the pharmaceutical composition is capable of enhancing, increasing, augmenting, and/or supplementing the levels of a Collagen alpha-1 (VII) chain polypeptide and/or a Lysyl hydroxylase 3 polypeptide and/or a Keratin type I cytoskeletal 17 polypeptide in one or more cells of the subject. In some examples, the pharmaceutical composition comprises a virus comprising the vector, wherein the vector comprises one or more transgenes encoding a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, a Keratin type I cytoskeletal 17 polypeptide, or a chimeric polypeptide thereof, and a pharmaceutically acceptable carrier. In some examples, the virus is an adenovirus, adeno-associated virus, retrovirus, lentivirus, sendai virus, herpes simplex virus, vaccinia virus, or any hybrid virus thereof. In some examples, the virus is replication-defective. In some examples, the virus is a herpes simplex virus (HSV). In some examples, the herpes simplex virus is a

herpes simplex type 1 virus, a herpes simplex type 2 virus, or any derivatives thereof. In some examples, the recombinant herpes simplex virus genome is a recombinant HSV-1 genome, a recombinant HSV-2 genome, or any derivatives thereof. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in an immediate early herpes simplex virus gene. In some examples, the herpes simplex virus gene is ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, or UL55. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP27, and UL55 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4, ICP22, ICP27, ICP47, and UL55 genes. In some examples, the inactivating mutation in the ICP4, ICP27, and UL55 genes is a deletion of the coding sequence of the ICP4, ICP27, and UL55 genes. In some examples, the inactivating mutation in the ICP22 and ICP47 genes is a deletion in the promoter region of the ICP22 and ICP47 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP4 and ICP22 genes. In some example, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0 and ICP4 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, and ICP22 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, and ICP27 genes. In some examples, the recombinant herpes simplex virus genome comprises an inactivating mutation in the ICP0, ICP4, ICP22, ICP27, and UL55 genes. In some examples, the inactivating mutation is a deletion of the coding sequence of the genes. In some examples, the recombinant herpes simplex virus genome further comprises an inactivating mutation in the ICP47 gene, an inactivating mutation in the UL41 gene, or an inactivation mutation in the ICP47 and UL41 genes. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more of the ICP4 viral gene loci. In some examples, the recombinant herpes simplex virus genome comprises the one or more transgenes within the UL41 viral gene locus. In some examples, the vector is capable of replicating within a target cell when delivered into said target cell. In some examples, the pharmaceutically acceptable carrier is suitable

for topical or transdermal administration. In some examples, the pharmaceutically acceptable carrier is suitable for subcutaneous or intradermal administration. In some examples, the one or more transgenes comprises an miRNA binding site. In some examples, the vector comprises a transgene encoding a Collagen alpha-1 (VII) chain polypeptide. In some examples, the vector comprises a transgene encoding a Lysyl hydroxylase 3 polypeptide. In some examples, the vector comprises a transgene encoding a Keratin type I cytoskeletal 17 polypeptide. In some examples, the Collagen alpha-1 (VII) chain polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 2. In some examples, the collagen alpha-1 (VII) chain polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 2. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Collagen alpha-1 (VII) chain polypeptide enhances, increases, augments, and/or supplements epithelial basement membrane organization and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 4. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements the formation of hydroxylysine residues on one or more collagen polypeptides of a subject when the Lysyl hydroxylase 3 polypeptide is expressed in one or more target cells of the subject. In some examples, the Lysyl hydroxylase 3 polypeptide enhances, increases, augments, and/or supplements anchoring fibril formation, epithelial basement membrane organization, and/or epithelial basement adherence of a subject when the polypeptide is expressed in one or more target cells of the subject. In some examples, the Keratin type I cytoskeletal 17 polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 30. In some examples, the Keratin type I cytoskeletal 17 polypeptide is a fragment, wherein the fragment has at least 100 consecutive amino acids of SEQ ID NO: 30. In some examples, the Keratin type I cytoskeletal 17 polypeptide enhances, increases, augments, and/or supplements wound healing in a subject. In some examples, the vector comprises

at least a first transgene and a second transgene. In some examples, the first transgene and the second transgene each encode a Collagen alpha-1 (VII) chain polypeptide. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide and the second transgene encodes a Lysyl hydroxylase 3 polypeptide. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide and the second transgene encodes a Keratin type I cytoskeletal 17 polypeptide. In some examples, the first transgene encodes a Lysyl hydroxylase 3 polypeptide and the second transgene encodes a Keratin type I cytoskeletal 17 polypeptide. In some examples, the vector comprises at least a first transgene, a second transgene, and a third transgene. In some examples, the first transgene encodes a Collagen alpha-1 (VII) chain polypeptide, the second transgene encodes a Lysyl hydroxylase 3 polypeptide, and the third transgene encodes a Keratin type I cytoskeletal 17 polypeptide. In some examples, the pharmaceutical composition is administered topically or transdermally to the subject. In some examples, the pharmaceutical composition is administered subcutaneously or intradermally to the subject. In some examples, the pharmaceutical composition is administered one, two three, four, five or more times per day. In some examples, the pharmaceutical composition is administered to one or more affected and/or unaffected areas of the subject. In some examples, the disease or disorder of the skin is one or more of epidermolysis bullosa, skin cancer, psoriasis, lichen planus, lupus, rosacea, eczema, cutaneous candidiasis, cellulitis, impetigo, decubitus ulcers, erysipelas, ichthyosis vulgaris, dermatomyositis, acrodermatitis, stasis dermatitis, nethertons syndrome, epidermolysis bullosa simplex (LAMB3 gene), autosomal recessive congenital ichthyosis, xeroderma pigmentosa, and pemphigoid.

[0018a] In another aspect, the present disclosure refers to the pharmaceutical composition as described herein for use as a medicament.

[0018b] In another aspect, the present disclosure refers to the pharmaceutical composition as described herein for use as a medicament to deliver the one or more transgenes to the skin of a subject.

[0018c] In another aspect, the present disclosure refers to the pharmaceutical composition as described herein for use in providing prophylactic, palliative, or therapeutic relief of a wound, disorder, or disease of the skin of a subject, wherein the subject suffers from epidermolysis bullosa.

[0018d] In another aspect, the present disclosure refers to use of the pharmaceutical composition as described herein in the manufacture of a medicament for providing prophylactic, palliative, or therapeutic relief of a wound, disorder, or disease of the skin of a subject, wherein the subject suffers from epidermolysis bullosa.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] **FIGS. 1A-F** show schematics of wild-type and modified herpes simplex virus genomes. **FIG. 1A** shows a wild-type herpes simplex virus genome. **FIG. 1B** shows a modified herpes simplex virus genome comprising a transgene encoding a Collagen alpha-1 (VII) chain polypeptide. **FIG. 1C** shows a modified herpes simplex virus genome comprising two transgenes, one encoding a Collagen alpha-1 (VII) chain polypeptide and the other encoding a Lysyl hydroxylase 3 polypeptide, with the transgenes encoded on the same strand of DNA. **FIG. 1D** shows a modified herpes simplex virus genome comprising two transgenes,one encoding a Collagen alpha-1 (VII) chain polypeptide and the other encoding a

CLAIMS

1. A pharmaceutical composition comprising:

    a) a replication-defective herpes simplex virus (HSV) comprising a recombinant herpes simplex virus genome, wherein the recombinant herpes simplex virus genome comprises one or more transgenes encoding a polypeptide selected from the group consisting of a Collagen alpha-1 (VII) chain polypeptide, a Lysyl hydroxylase 3 polypeptide, and a Keratin type I cytoskeletal 17 polypeptide; and

    b) a pharmaceutically acceptable carrier.

2. The pharmaceutical composition of claim 1, wherein the Collagen alpha-1 (VII) chain polypeptide has at least 80% sequence identity to the sequence of SEQ ID NO: 2.

3. The pharmaceutical composition of claim 1 or claim 2, wherein the Collagen alpha-1 (VII) chain polypeptide has at least 95% sequence identity to the sequence of SEQ ID NO: 2.

4. The pharmaceutical composition of any one of claims 1-3, wherein the pharmaceutically acceptable carrier is suitable for a route of administration selected from the group consisting of topical administration, transdermal administration, subcutaneous administration, intradermal administration, and any combinations thereof.

5. A pharmaceutical composition useful for delivery of one or more transgenes to the skin of a subject, comprising:

    a) a replication-defective herpes simplex virus (HSV) comprising a recombinant herpes simplex virus genome, wherein the recombinant herpes simplex virus genome comprises one or more polynucleotides encoding the one or more transgenes; and

    b) a pharmaceutically acceptable carrier;

wherein the pharmaceutical composition is a topical, transdermal, subcutaneous, or intradermal composition; and

wherein the replication-defective HSV is suitable for delivering the one or more polynucleotides encoding the one or more transgenes to one or more target cells of the epidermis and/or dermis of the subject.

6. The pharmaceutical composition of any one of claims 1-5, wherein the herpes simplex virus (HSV) is a herpes simplex type 1 virus or a herpes simplex type 2 virus.

7. The pharmaceutical composition of any one of claims 1-6, wherein the herpes simplex virus (HSV) is a herpes simplex type 1 virus (HSV-1).

8. The pharmaceutical composition of any one of claims 1-7, wherein the recombinant herpes simplex virus genome comprises an inactivating mutation.

9. The pharmaceutical composition of claim 8, wherein the inactivating mutation is in at least one herpes simplex virus gene selected from the group consisting of ICP0, ICP4, ICP22, ICP27, ICP47, tk, UL41, and UL55.

10. The pharmaceutical composition of any one of claims 1-9, wherein the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more viral gene loci.

11. The pharmaceutical composition of any one of claims 1-10, wherein the recombinant herpes simplex virus genome comprises the one or more transgenes within one or more of the ICP4 viral gene loci.

12. The pharmaceutical composition of any one of claims 5-11, wherein the one or more transgenes encode a Collagen alpha-1 (VII) chain polypeptide having at least 80% sequence identity to the sequence of SEQ ID NO: 2.

13. The pharmaceutical composition of any one of claims 5-12, wherein the one or more transgenes encode a Collagen alpha-1 (VII) chain polypeptide having at least 95% sequence identity to the sequence of SEQ ID NO: 2.

14. The pharmaceutical composition of any one of claims 1-13, wherein the HSV has reduced cytotoxicity as compared to a wild-type herpes simplex virus.

15. The pharmaceutical composition of any one of claims 1-14 for use as a medicament.

16. The pharmaceutical composition of any one of claims 1-14 for use as a medicament to deliver the one or more transgenes to the skin of a subject.

17. The pharmaceutical composition of any one of claims 1-14 for use in providing prophylactic, palliative, or therapeutic relief of a wound, disorder, or disease of the skin of a subject, wherein the subject suffers from epidermolysis bullosa.

18. Use of the pharmaceutical composition of any one of claims 1-14 in the manufacture of a medicament for providing prophylactic, palliative, or therapeutic relief of a wound, disorder, or disease of the skin of a subject, wherein the subject suffers from epidermolysis bullosa.

19. The pharmaceutical composition for use of claim 17, or the use of claim 18, wherein the pharmaceutical composition is to be administered topically, transdermally, subcutaneously, or intradermally to the subject.

20. The pharmaceutical composition for use of claim 17, or the use of claim 18, wherein the pharmaceutical composition is to be administered topically to the subject.

21. The pharmaceutical composition for use of claim 16 or claim 17, or the use of any one of claims 18-20, wherein the subject is a human.