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(54) **GENE THERAPY FOR RECESSIVE DYSTROPHIC EPIDERMOLYSIS BULLOSA USING GENETICALLY CORRECTED AUTOLOGOUS KERATINOCTYES**

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said application No. 18/933,687 is a continuation of application No. 16/066,253, filed on Jun. 26, 2018, filed as application No. PCT/US2017/012061 on Jan. 3, 2017, now Pat. No. 12,173,314.

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**Publication Classification**

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*A61K 48/00* (2006.01)

(52) **U.S. Cl.**

CPC ..... *C12N 5/0629* (2013.01); *A61K 48/0058* (2013.01); *A61K 48/0075* (2013.01); *A61K 48/0091* (2013.01); *C12N 2510/00* (2013.01); *C12N 2760/16043* (2013.01)

(57) **ABSTRACT**

Methods are provided for the cell-based delivery of collagen VII for the treatment of Epidermolysis Bullosa and corneal erosion. The disclosure also provides a composition and a pharmaceutical composition comprises, comprise, or alternatively consist essentially of, or yet further consist of a keratinocyte sheet or a corneal cell sheet.

**Specification includes a Sequence Listing.**

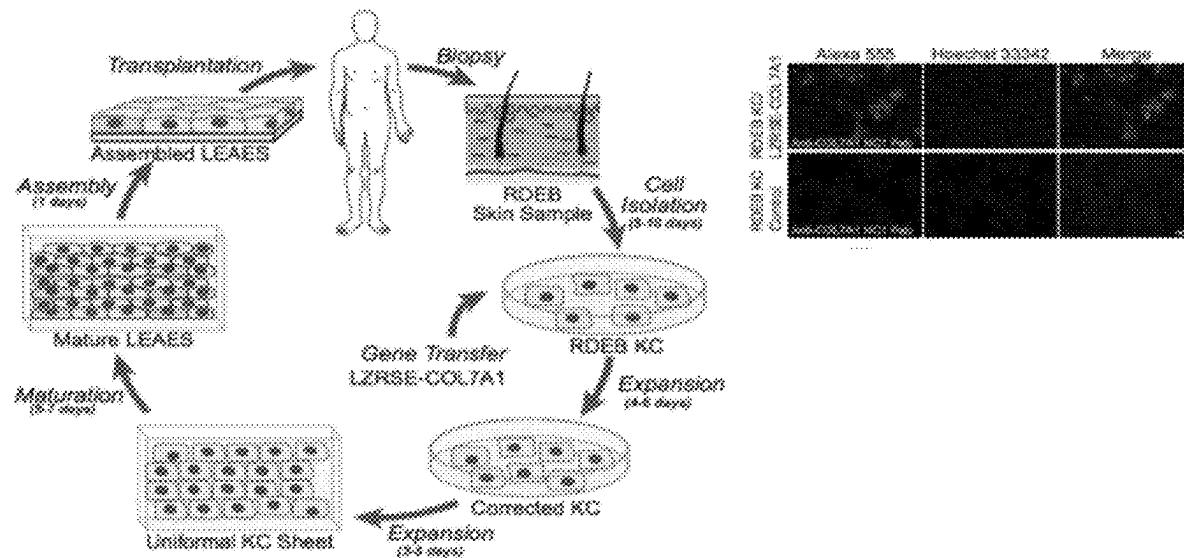


FIG. 1A

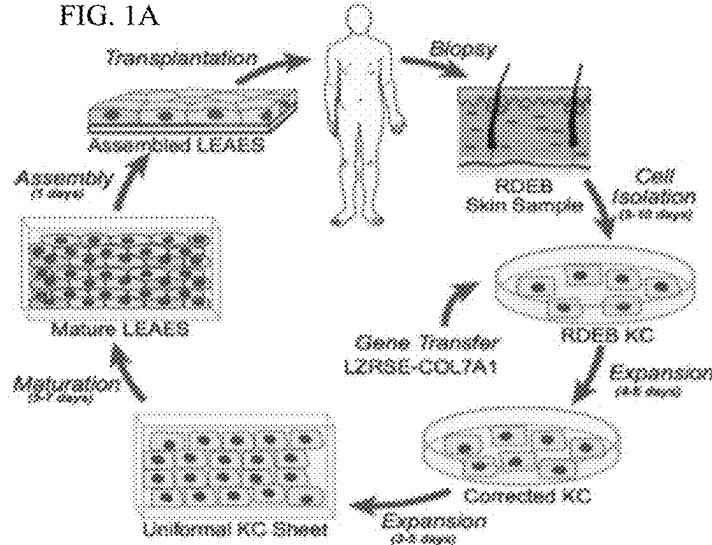


FIG. 1B

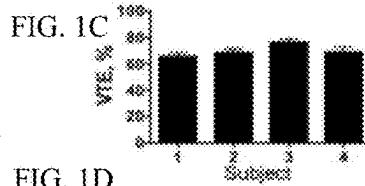
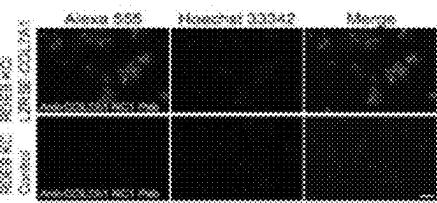


FIG. 1D



FIG. 1E

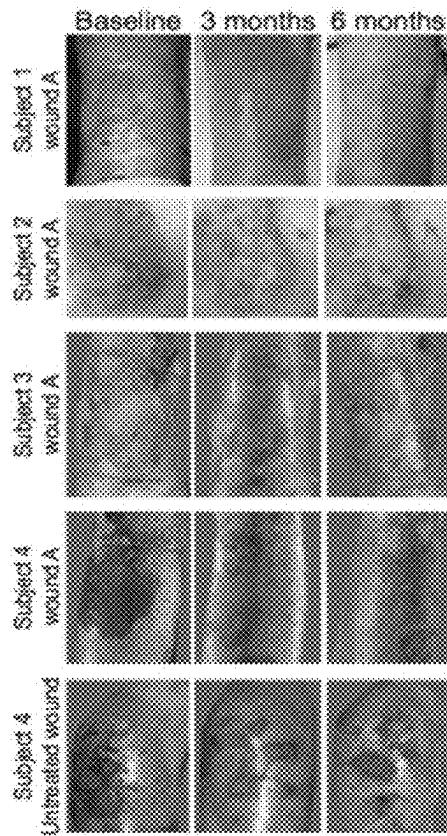


FIG. 1F

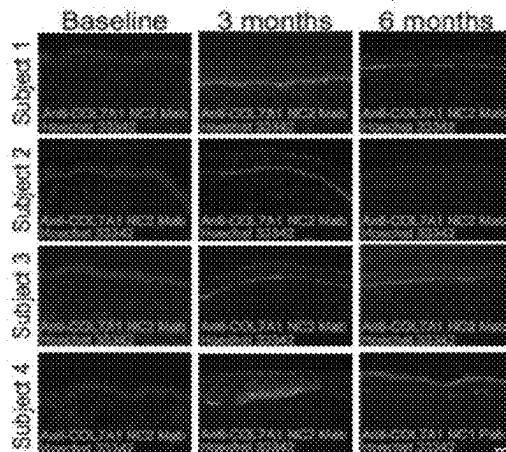
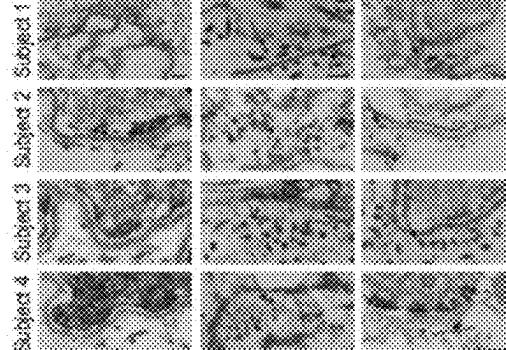


FIG. 1G Baseline 3 months 6 months



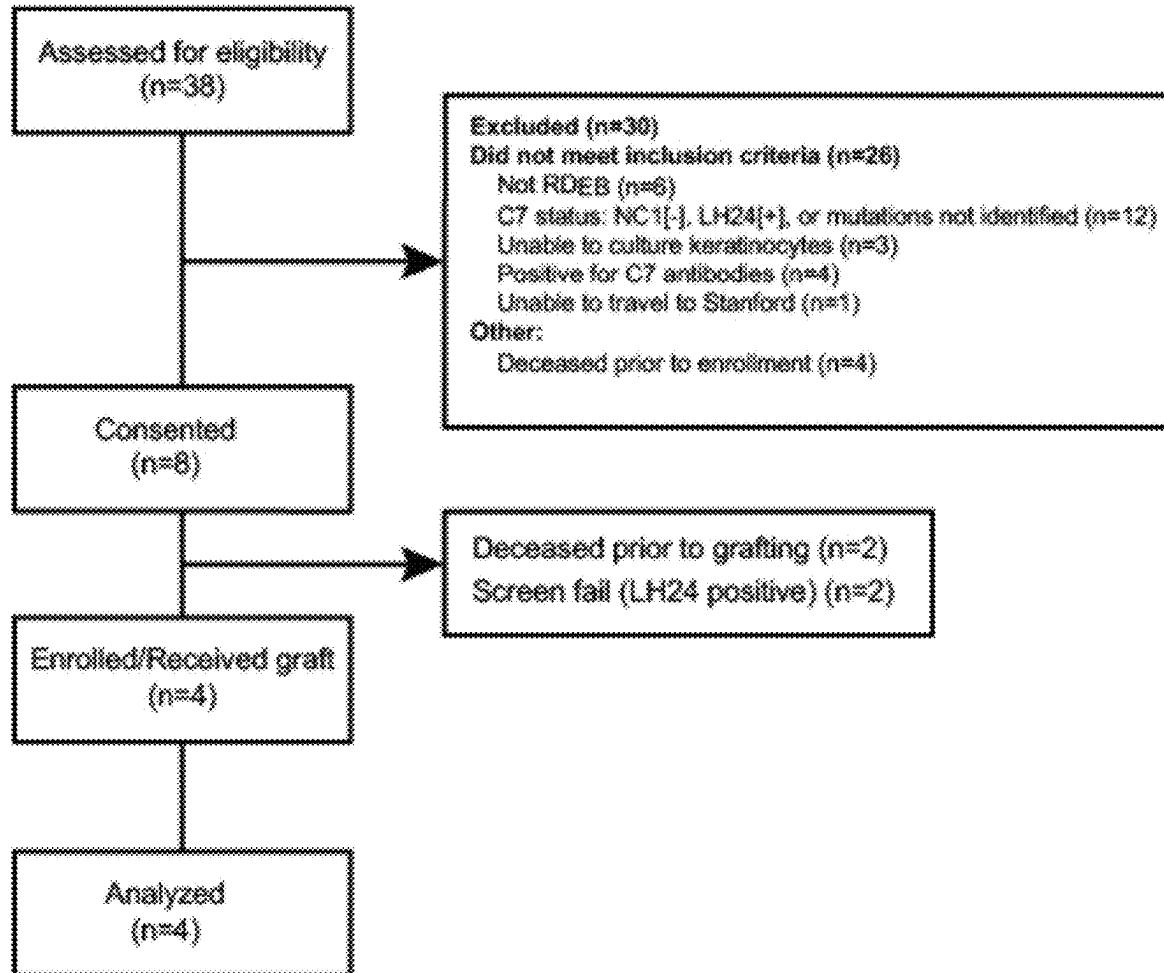


FIG. 2

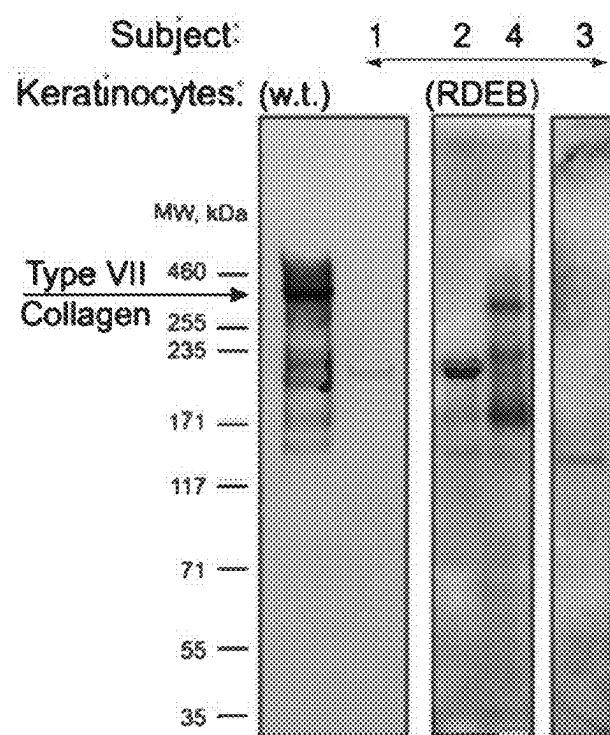


FIG. 3

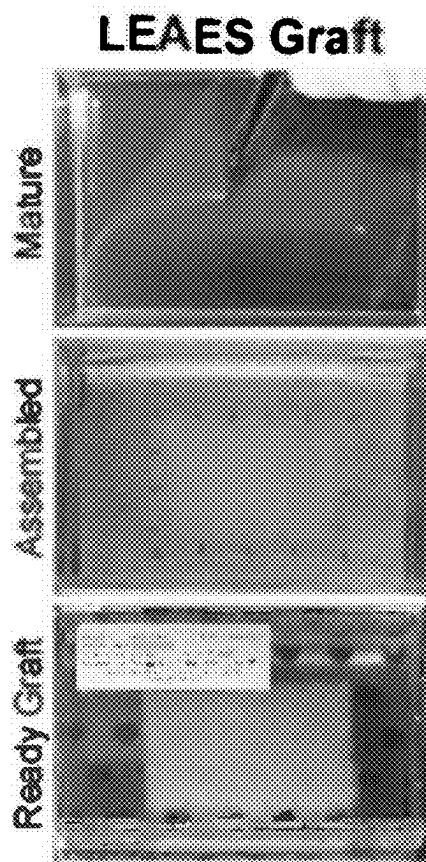


FIG. 4

FIG. 5A

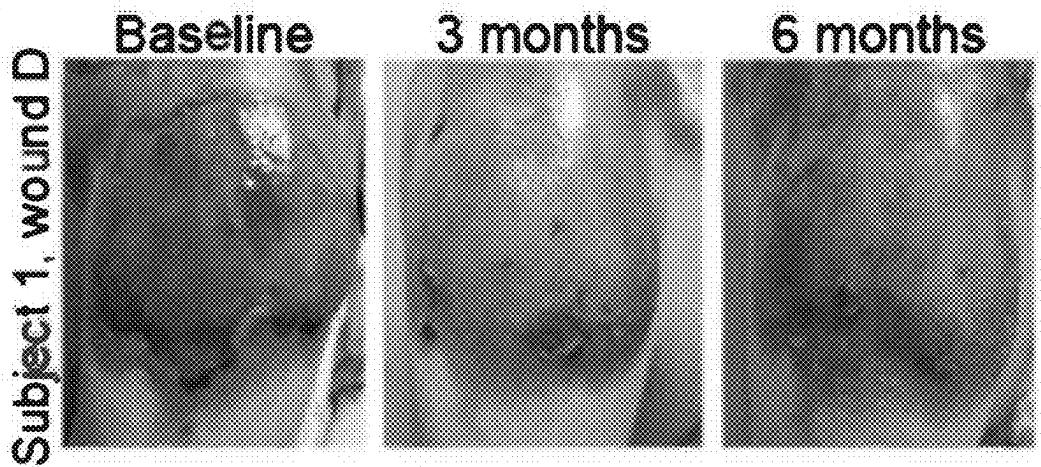


FIG. 5B

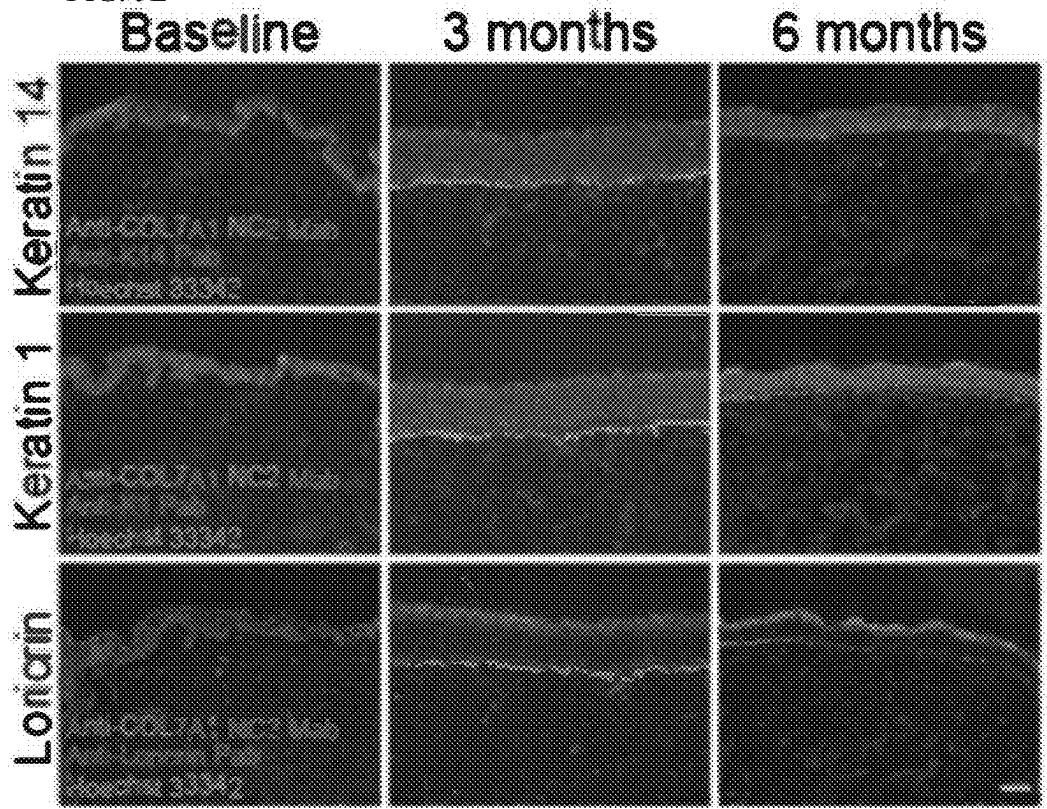


FIG. 6A

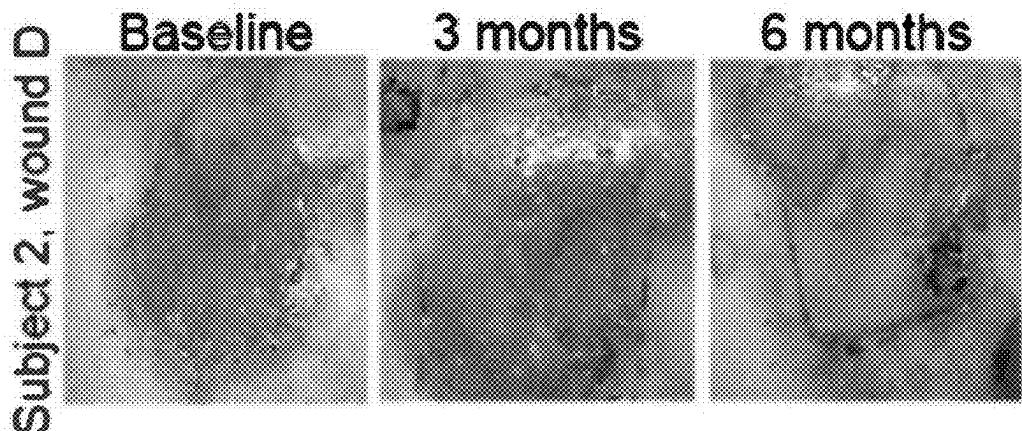


FIG. 6B

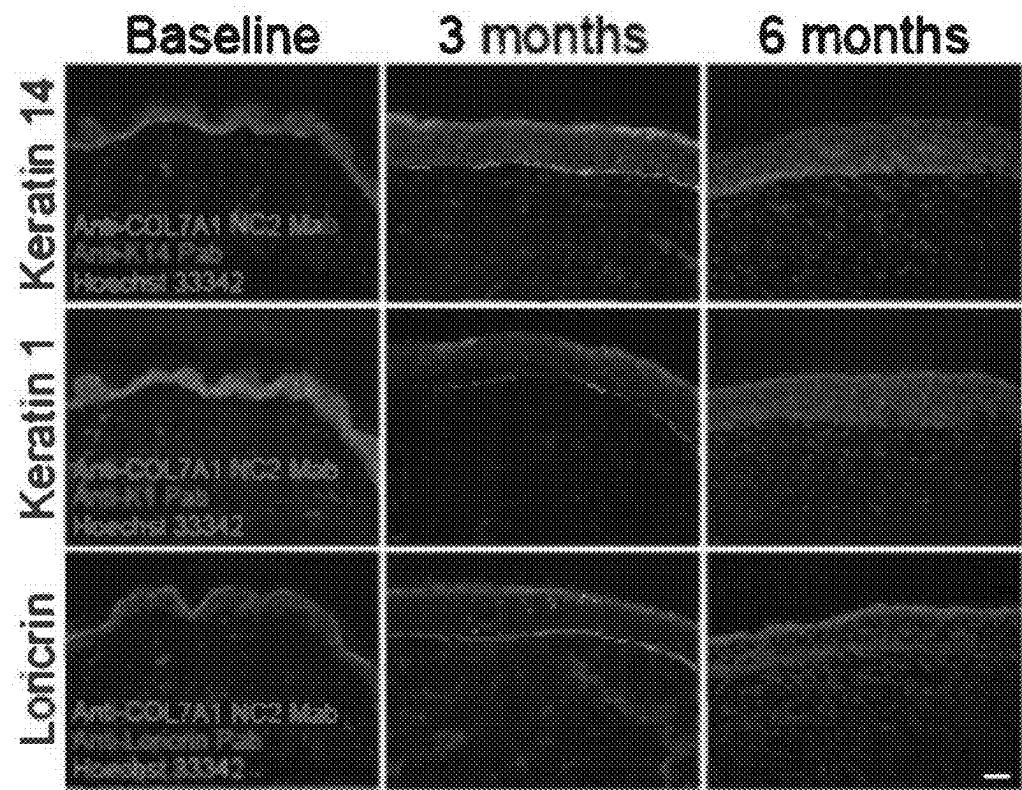


FIG. 7A

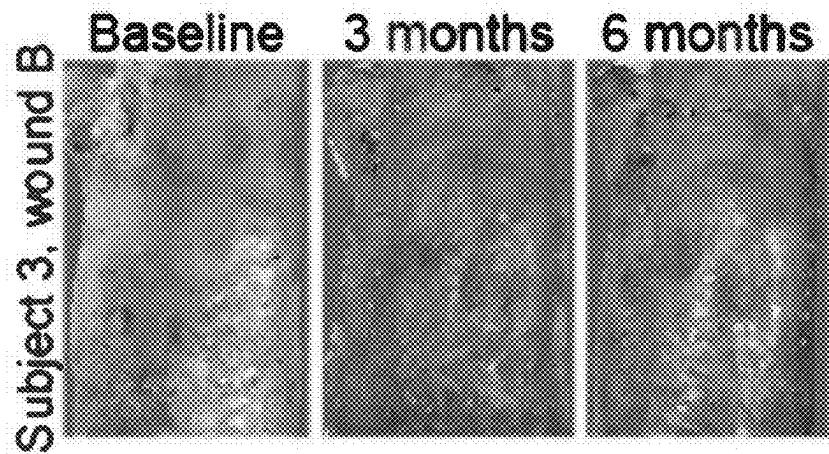


FIG. 7B

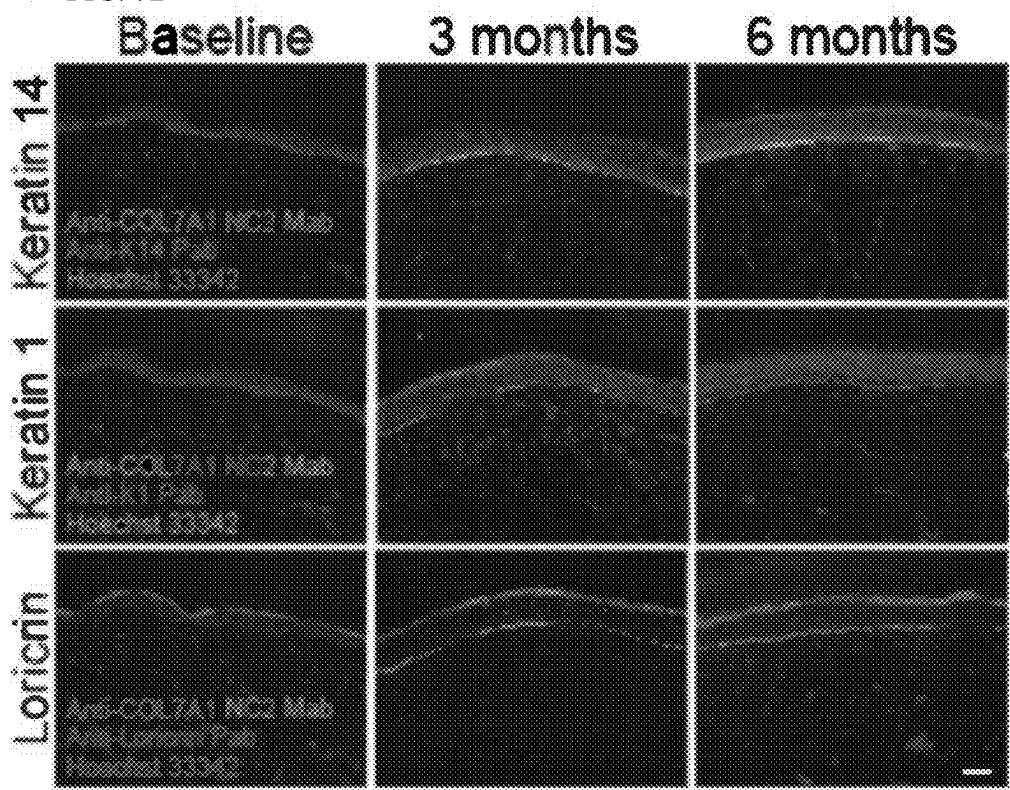


FIG. 8A

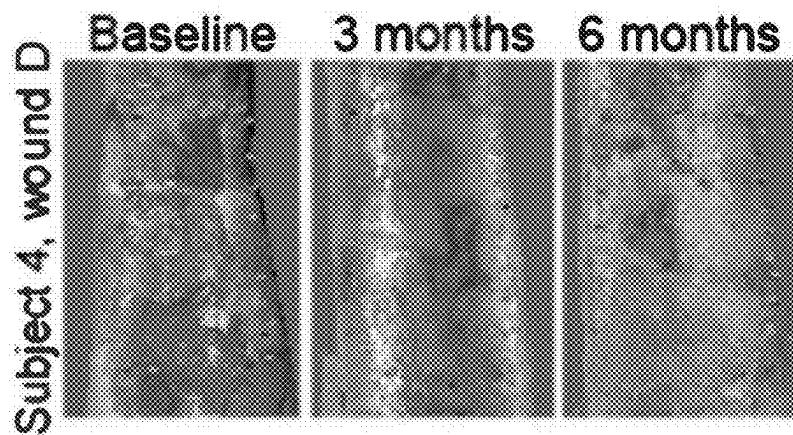
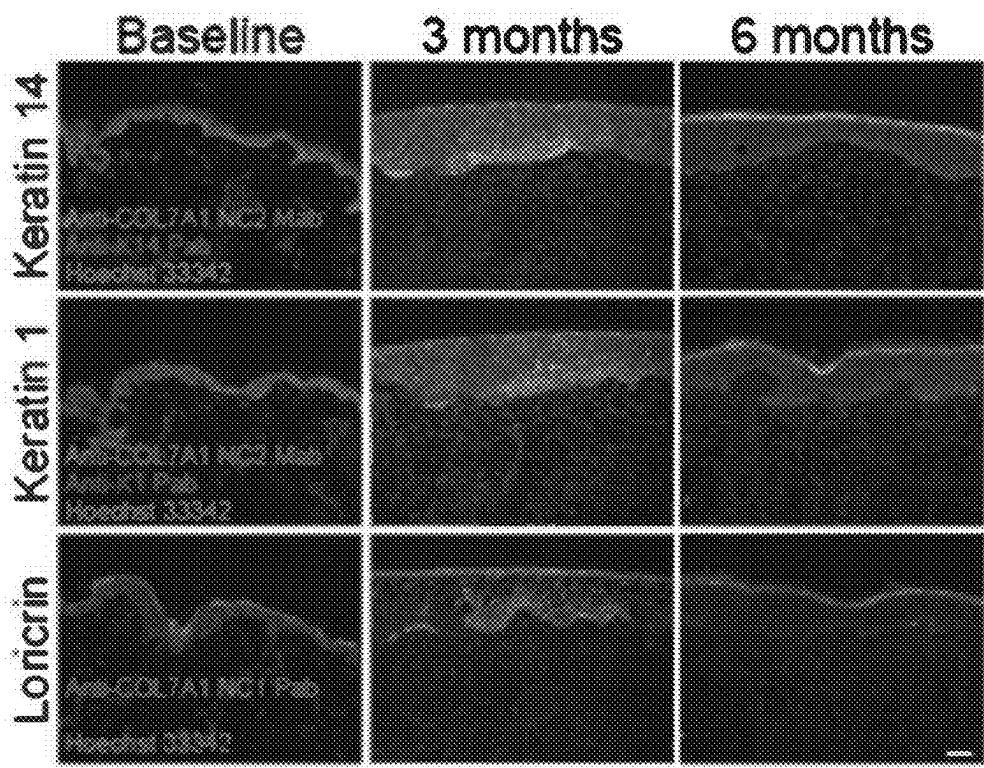


FIG. 8B



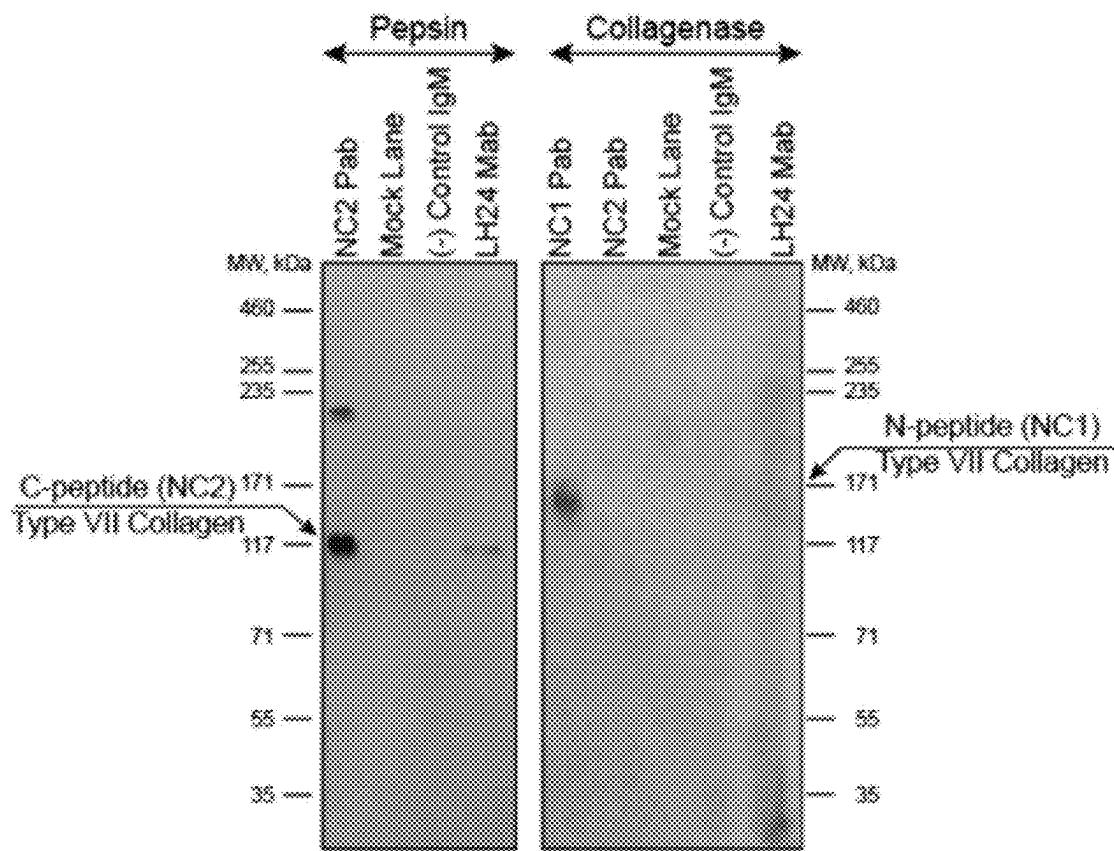


FIG. 9

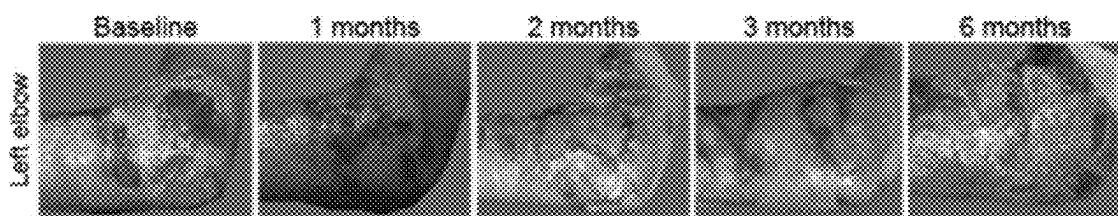


FIG. 10

FIG. 11A

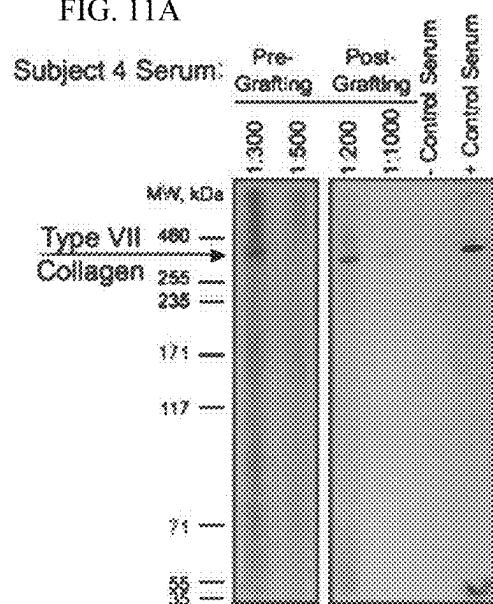
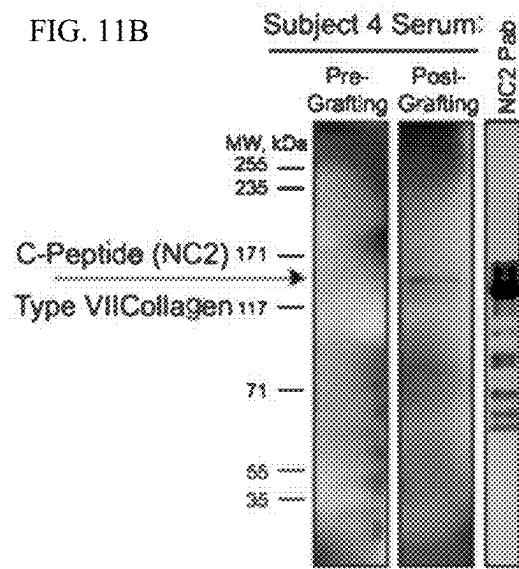


FIG. 11B



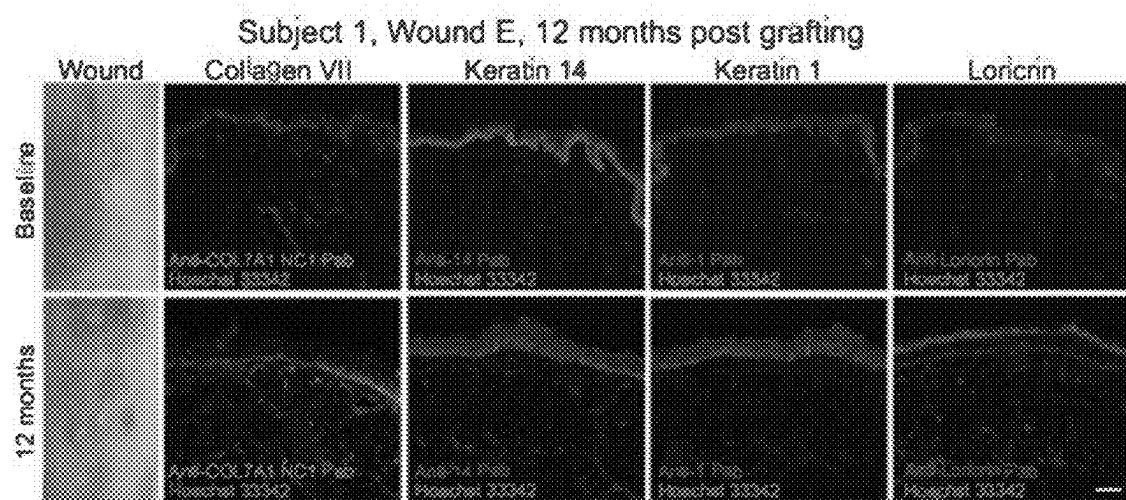


FIG. 12

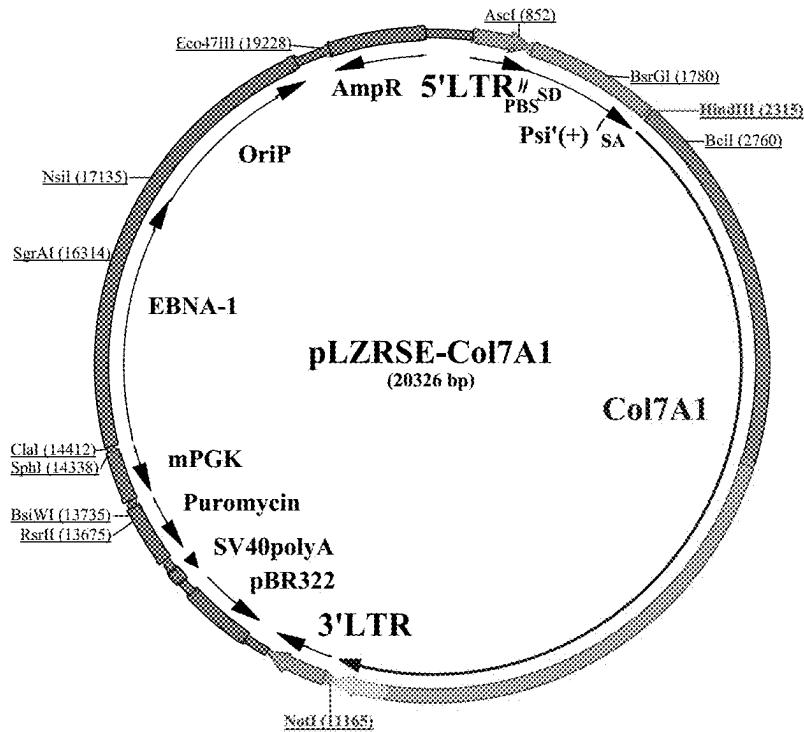


FIG. 13

Plasmid futures:

**5'LTR (409-1000bp)** – MoMuLV 5'LTR

**Psi'(+)(1001-2287bp)** – ORF reduced extended packaging signal  $\Psi'$

**PBS (1001-1018bp)** – retrovirus primer binding site

**SD (1058-1062bp)** – splice donor

**SA (1091-1093bp)** – splice acceptor

**Col7A1 (ORF 2325-11157bp)** – Type VII collagen

**3'LTR (11232-11849bp)** – MoMuLV 3'LTR

**pBR322 (12789-12088bp)** – pBR322 *E. coli* origin of replication

**SV40polyA (13075-12932bp)** – SV40 polyadenylation signal

**Puromycin (13797-13201bp)** – puromycin resistance gene for selection in eukaryotes

**mPGK (14383-13878bp)** – mouse phosphoglycerol kinase-1 promoter

**EBNA-1 (14432-17031BP)** – Epstein-Barr virus nuclear antigen 1

**OriP (17033-18962bp)** – Epstein-Barr virus origin of replication

**AmpR (20266-19310bp)** - *bla* gene for ampicillin selection in prokaryotes

FIG. 14

Subject	Site	Location	Description	Wound history	1 month <sup>2</sup>	3 months	6 months
1	A	R distal forearm	Erosion	>5 yrs			
	B	L forearm	Erosion	>5 yrs			
	C	R proximal forearm	Erosion	>5 yrs			
	D	R shoulder	Inflamed erosion	>5 yrs			
	E	L arm	New blister	1 wk			
	Z	R arm	Induced wound	New			
2	A	Central chest	Erosion	>5 yrs			
	B	L shoulder	Erosion and scar	>5 yrs			
	C	R forearm	Erosion and scar	3-5 yrs			
	D	R posterior shoulder	Inflamed erosion	>5 yrs			
	E	Lower back	Erosion	>5 yrs			
	Z	R upper chest	Induced wound	New			

FIG. 14 (Cont. 1)

3	A	R lateral hand	Erosion	3-5 yrs				
	B	R medial hand	Scar tissue	3-5 yrs				
	C	L ventral foot	Erosion and scar	3-5 yrs				
	D	L hand	Scar tissue	3-5 yrs				
	E	R foot	Erosion and scar	3-5 yrs				
	Z	L ventral foot	Induced wound	New				
4	A	L distal forearm	Inflamed erosion	>5 yrs				
	B	L medial forearm	Inflamed erosion	>5 yrs				
	C	L proximal forearm	Inflamed erosion	>5 yrs				
	D	R lateral forearm	Inflamed erosion	>5 yrs				
	E	R distal forearm	Inflamed erosion	>5 yrs				
	Z	R medial forearm	Induced wound	New				











































