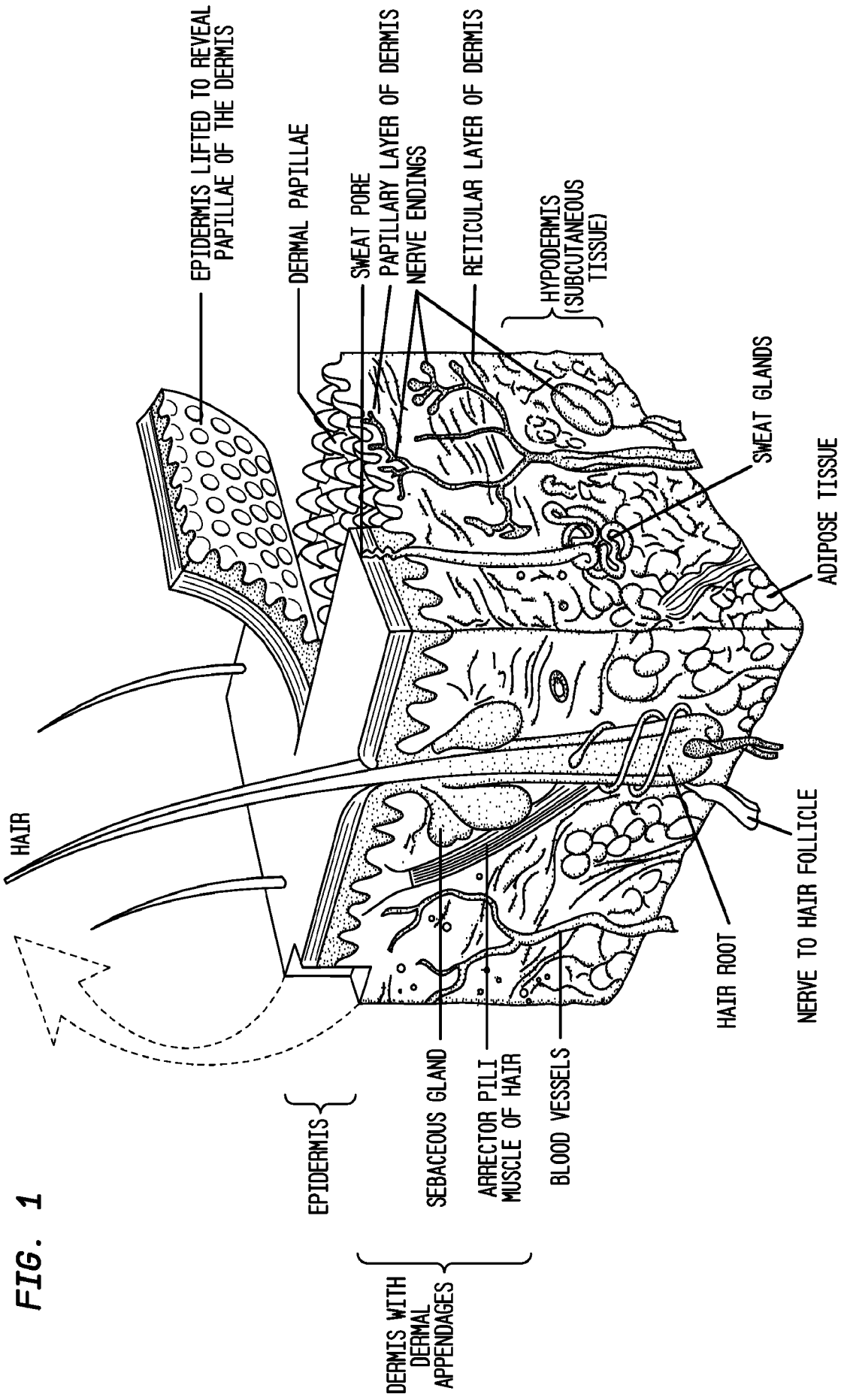
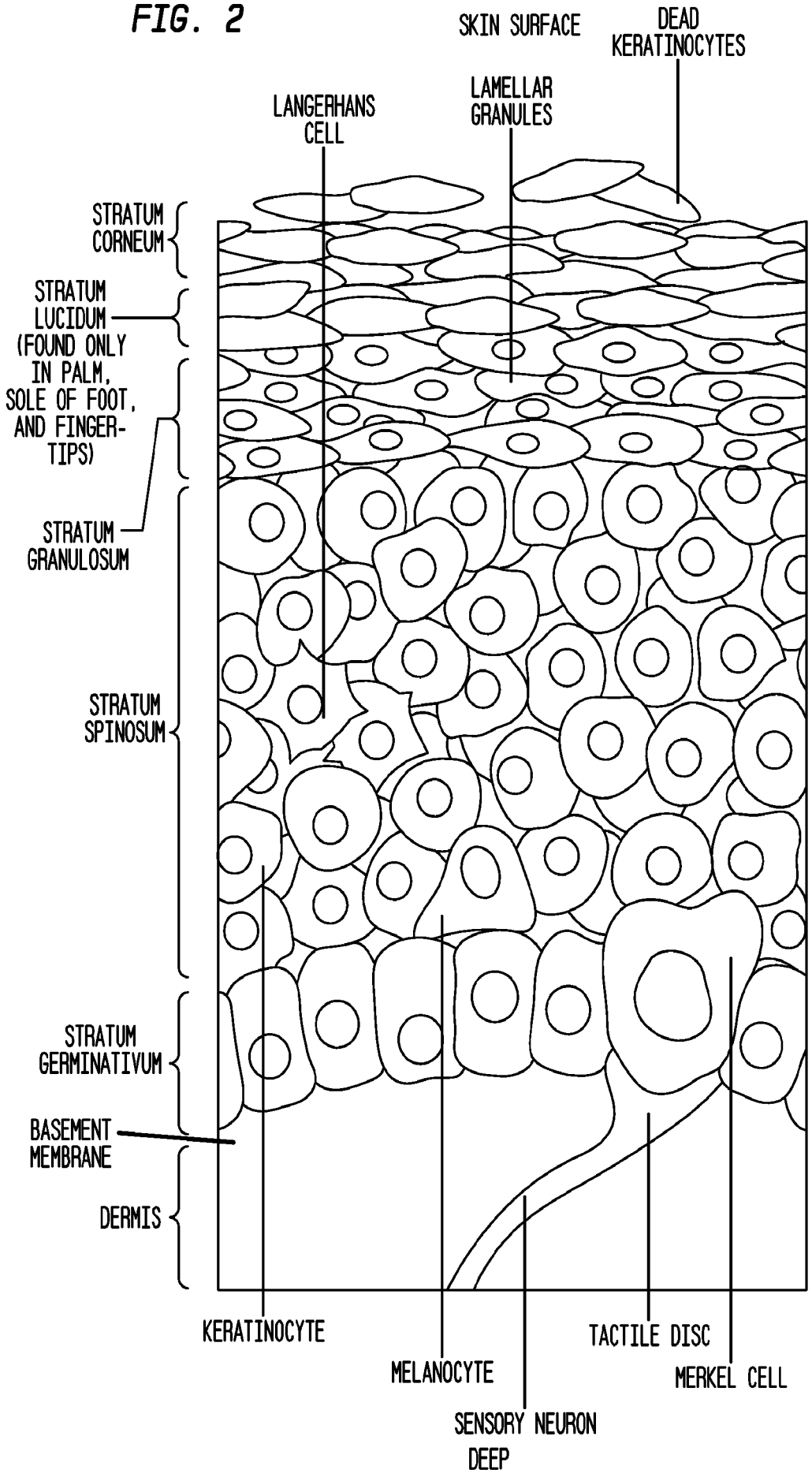

EPIDERMIS LIFTED TO REVEAL PAPILLAE OF THE DERMIS
DERMAL PAPILLAE
SWEAT PORE
PAPILLARY LAYER OF DERMIS
NERVE ENDINGS
RETICULAR LAYER OF DERMIS
HYPODERMIS (SUBCUTANEOUS TISSUE)
SWEAT GLANDS
ADIPOSE TISSUE
HAIR
HAIR ROOT
NERVE TO HAIR FOLLICLE
EPIDERMIS
SEBACEOUS GLAND
ARRECTOR PILI MUSCLE OF HAIR
BLOOD VESSELS
DERMIS WITH DERMAL APPENDAGES

FIG. 1

FIG. 2


SKIN SURFACE
DEAD KERATINOCYTES
LANGERHANS CELL
LAMELLAR GRANULES
STRATUM CORNEUM
STRATUM LUCIDUM (FOUND ONLY IN PALM, SOLE OF FOOT, AND FINGER-TIPS)
STRATUM GRANULOSUM
STRATUM SPINOSUM
STRATUM GERMINATIVUM
BASEMENT MEMBRANE
DERMIS
KERATINOCYTE
MELANOCYTE
SENSORY NEURON
DEEP
TACTILE DISC
MERKEL CELL

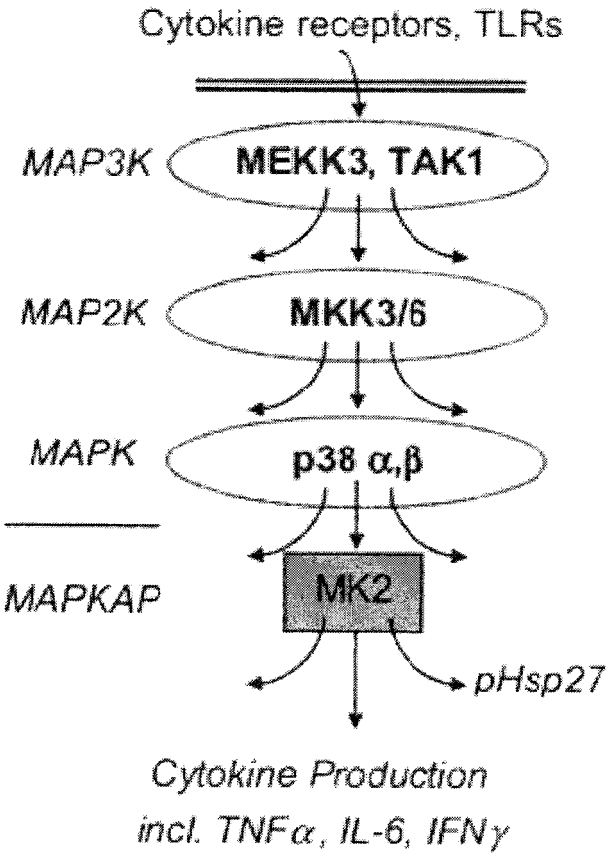

Cytokine receptors, TLRs
MAP3K
MEKK3, TAK1
MAP2K
MKK3/6
MAPK
p38 α,β
MAPKAP
MK2
pHsp27
Cytokine Production
incl. TNFα, IL-6, IFNγ

FIGURE 3

FIG. 4

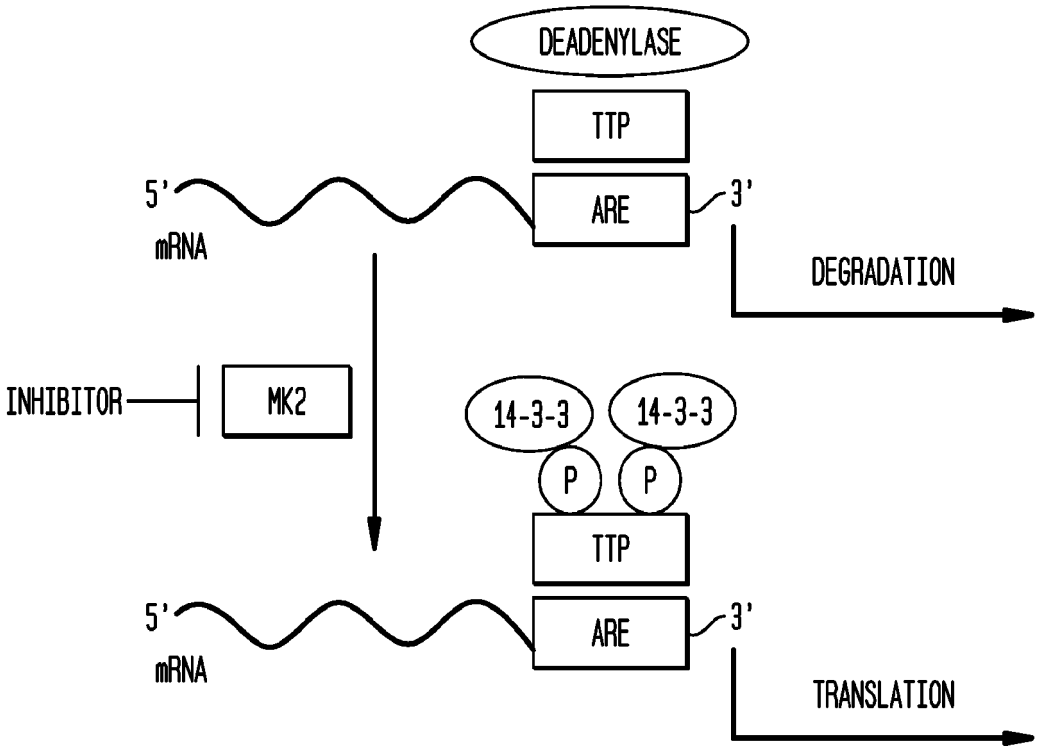
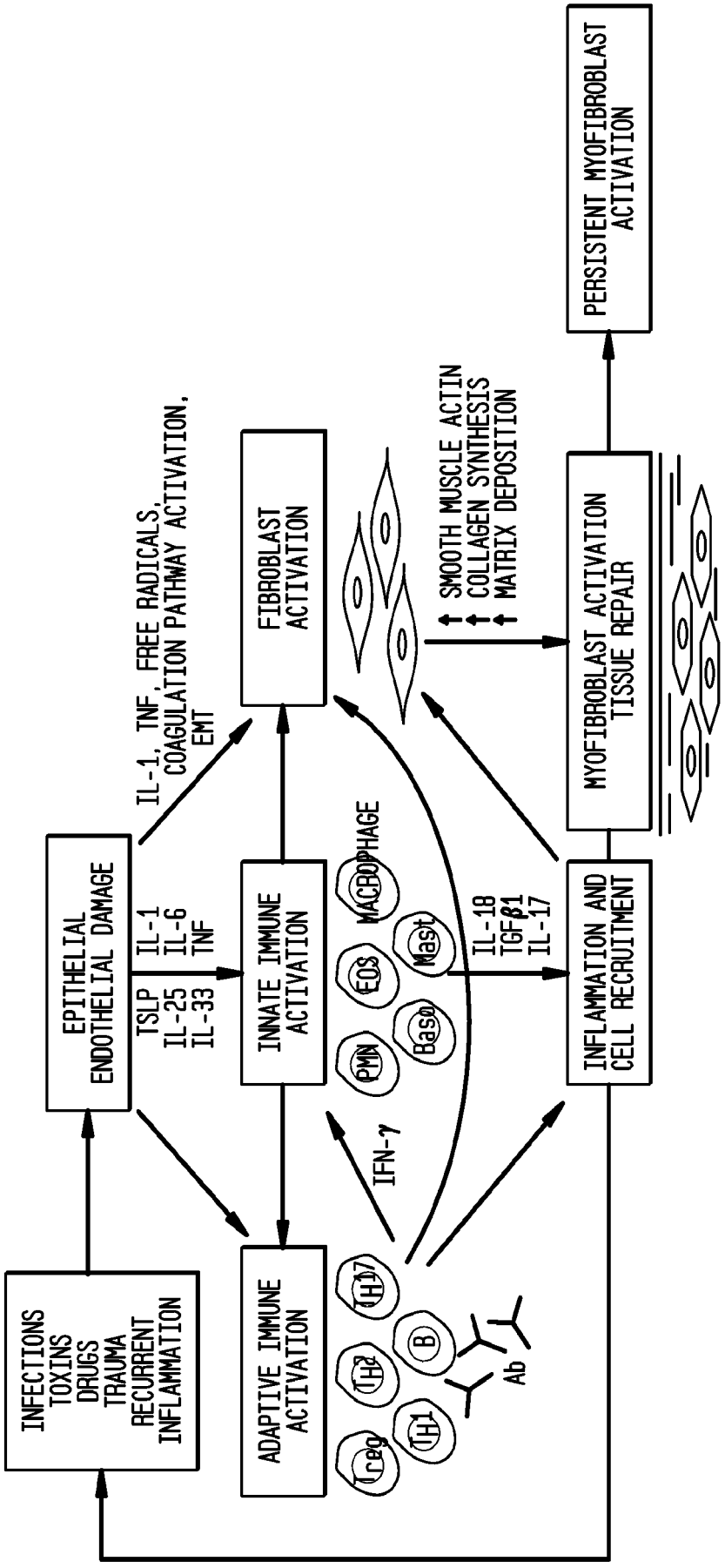

DEADENYLASE
TTP
5'
ARE
3'
mRNA
DEGRADATION
INHIBITOR
MK2
14-3-3
14-3-3
P
P
TTP
5'
ARE
3'
mRNA
TRANSLATION

FIG. 5


INFECTIONS
TOXINS
DRUGS
TRAUMA
RECURRENT
INFLAMMATION
EPITHELIAL
ENDOTHELIAL DAMAGE
TSLP
IL-25
IL-33
IL-1
IL-6
TNF
IL-1, TNF, FREE RADICALS,
COAGULATION PATHWAY ACTIVATION,
EMT
INNATE IMMUNE
ACTIVATION
ADAPTIVE IMMUNE
ACTIVATION
FIBROBLAST
ACTIVATION
MACROPHAGE
EOS
Mast
PMN
Baso
IFN-γ
Treg
TH1
TH2
TH17
B
Ab
IL-1B
TGFβ1
IL-17
SMOOTH MUSCLE ACTIN
COLLAGEN SYNTHESIS
MATRIX DEPOSITION
INFLAMMATION AND
CELL RECRUITMENT
MYOFIBROBLAST ACTIVATION
TISSUE REPAIR
PERSISTENT MYOFIBROBLAST
ACTIVATION

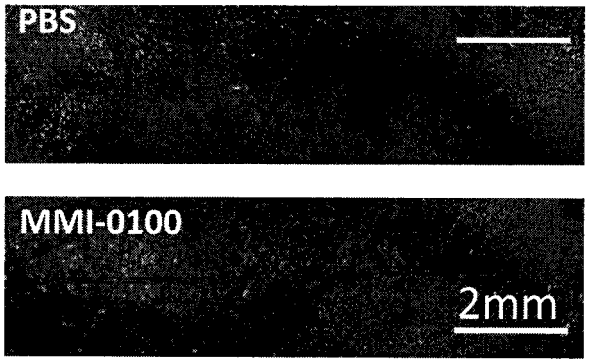


FIGURE 6

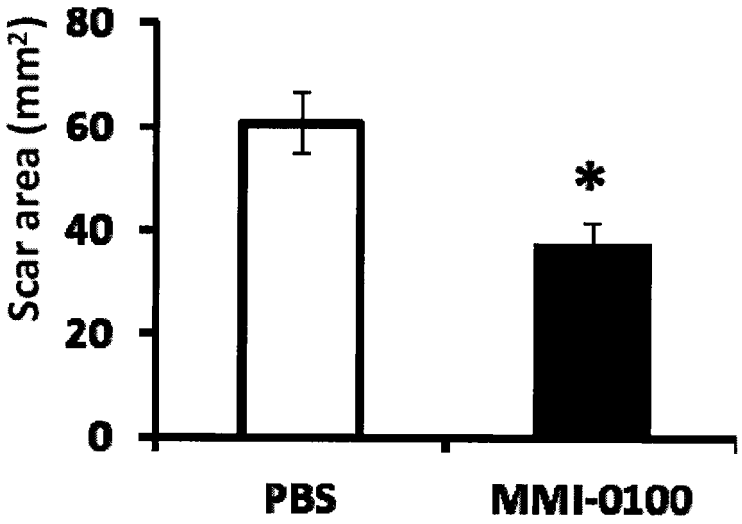


FIGURE 7

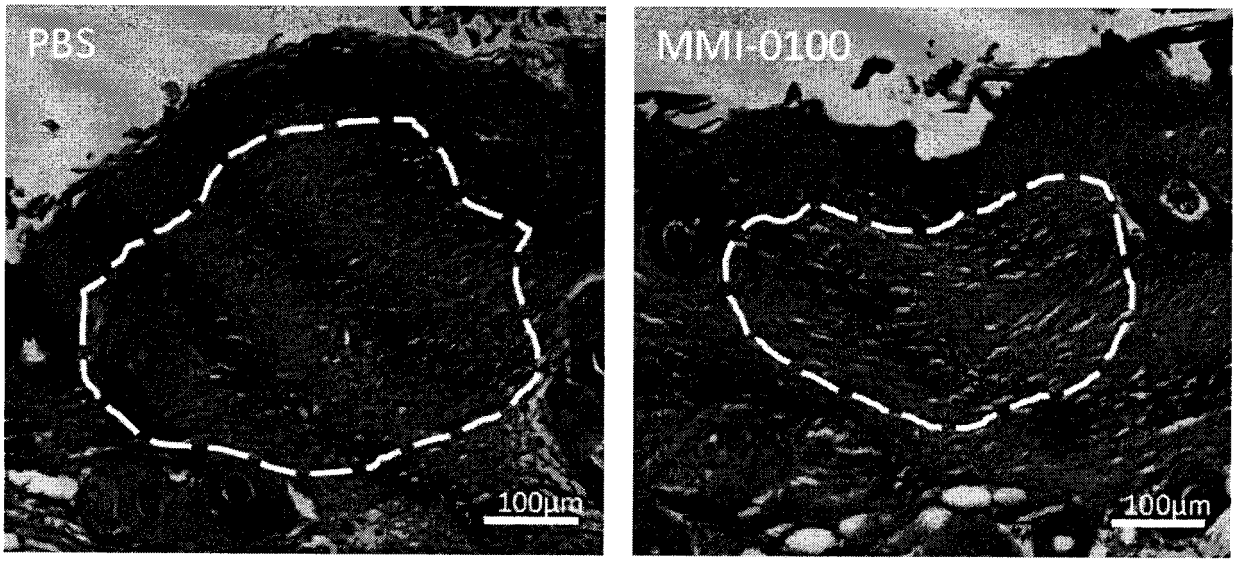


FIGURE 8

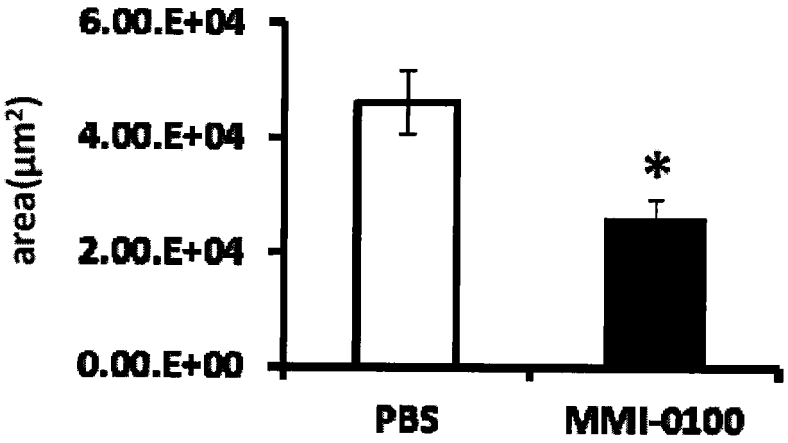


FIGURE 9

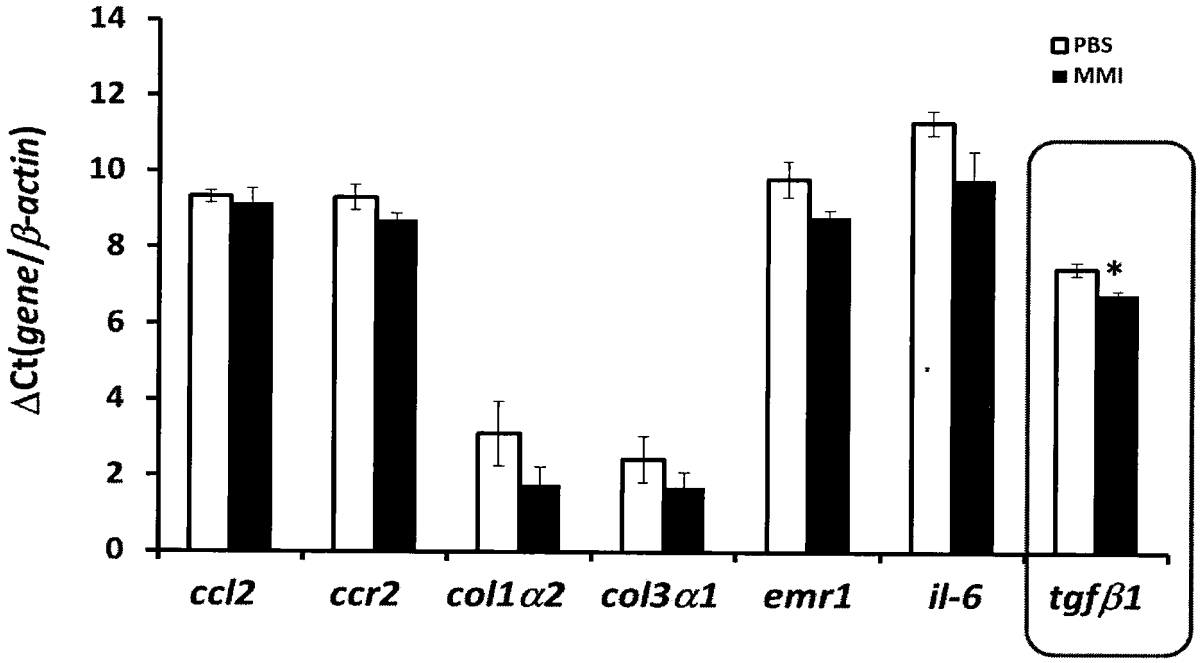

14
12
10
8
6
4
2
0
ΔCt(gene/β-actin)
PBS
MMI
*
ccl2
ccr2
col1α2
col3α1
emr1
il-6
tgfβ1

FIGURE 10

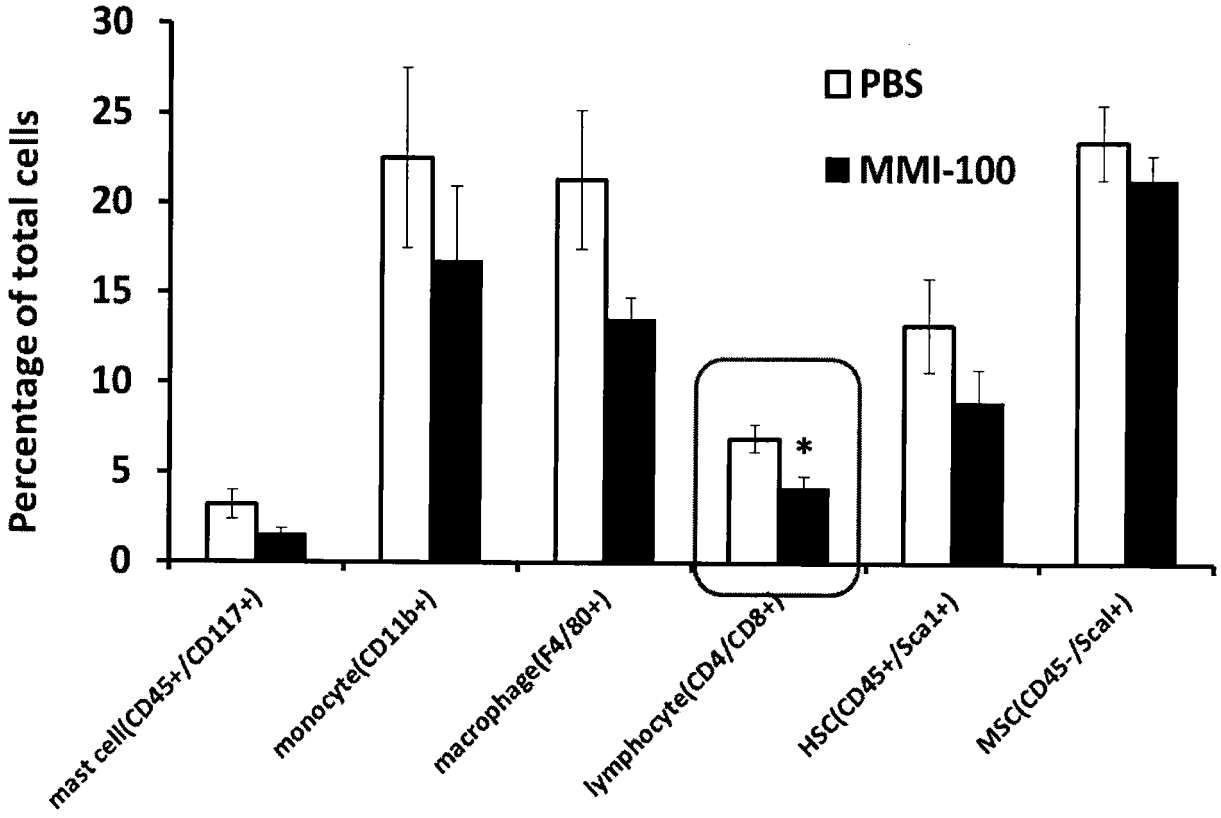

30
25
20
15
10
5
0
Percentage of total cells
PBS
MMI-100
*
mast cell(CD45+/CD117+)
monocyte(CD11b+)
macrophage(F4/80+)
lymphocyte(CD4/CD8+)
HSC(CD45+/Sca1+)
MSC(CD45-/Scal+)

FIGURE 11

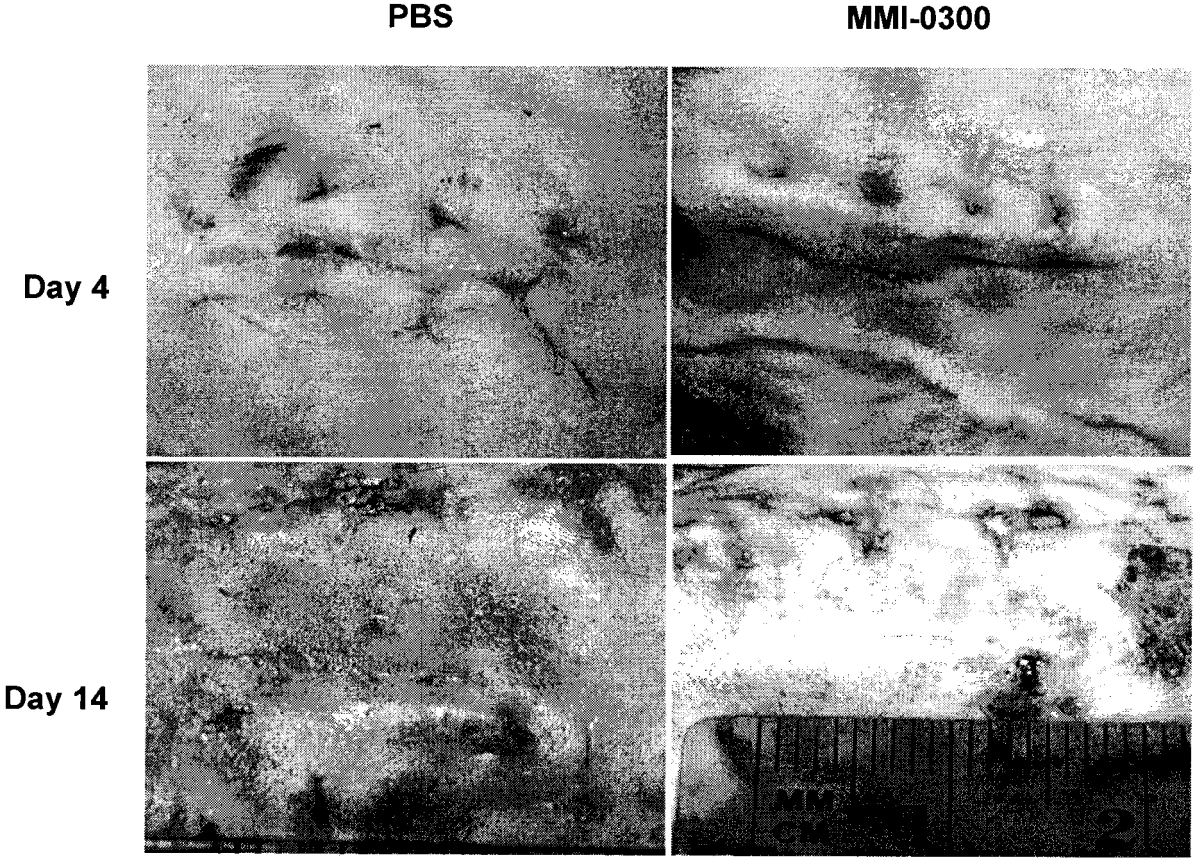


FIGURE 12

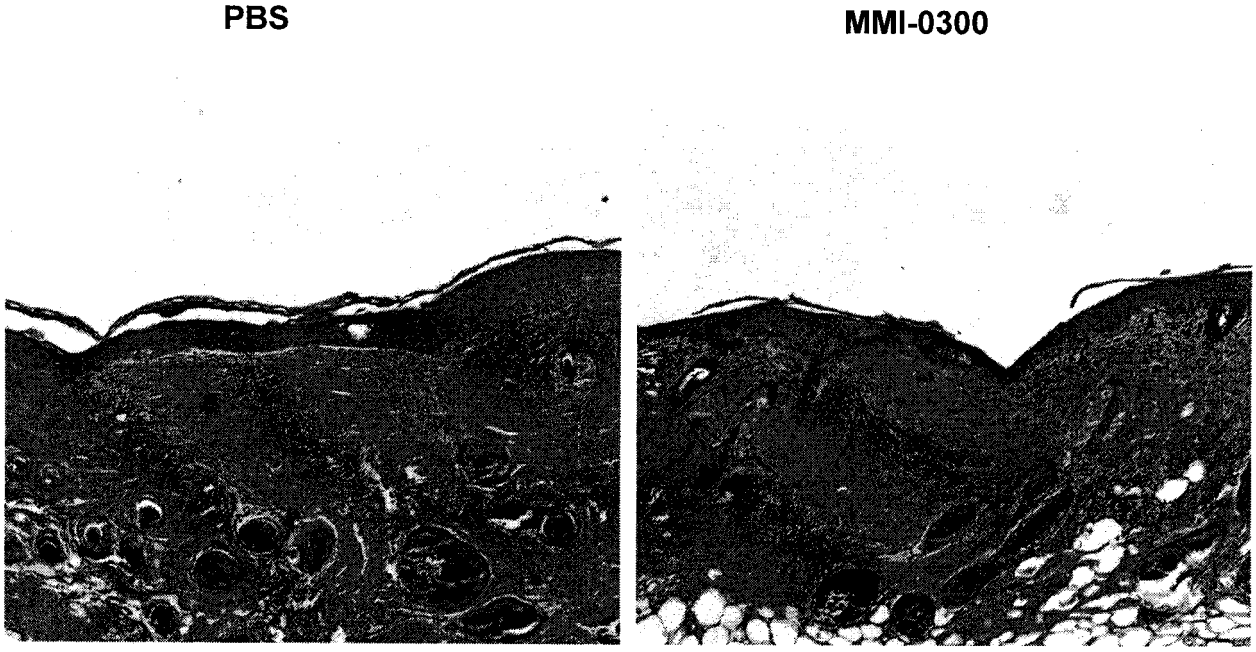
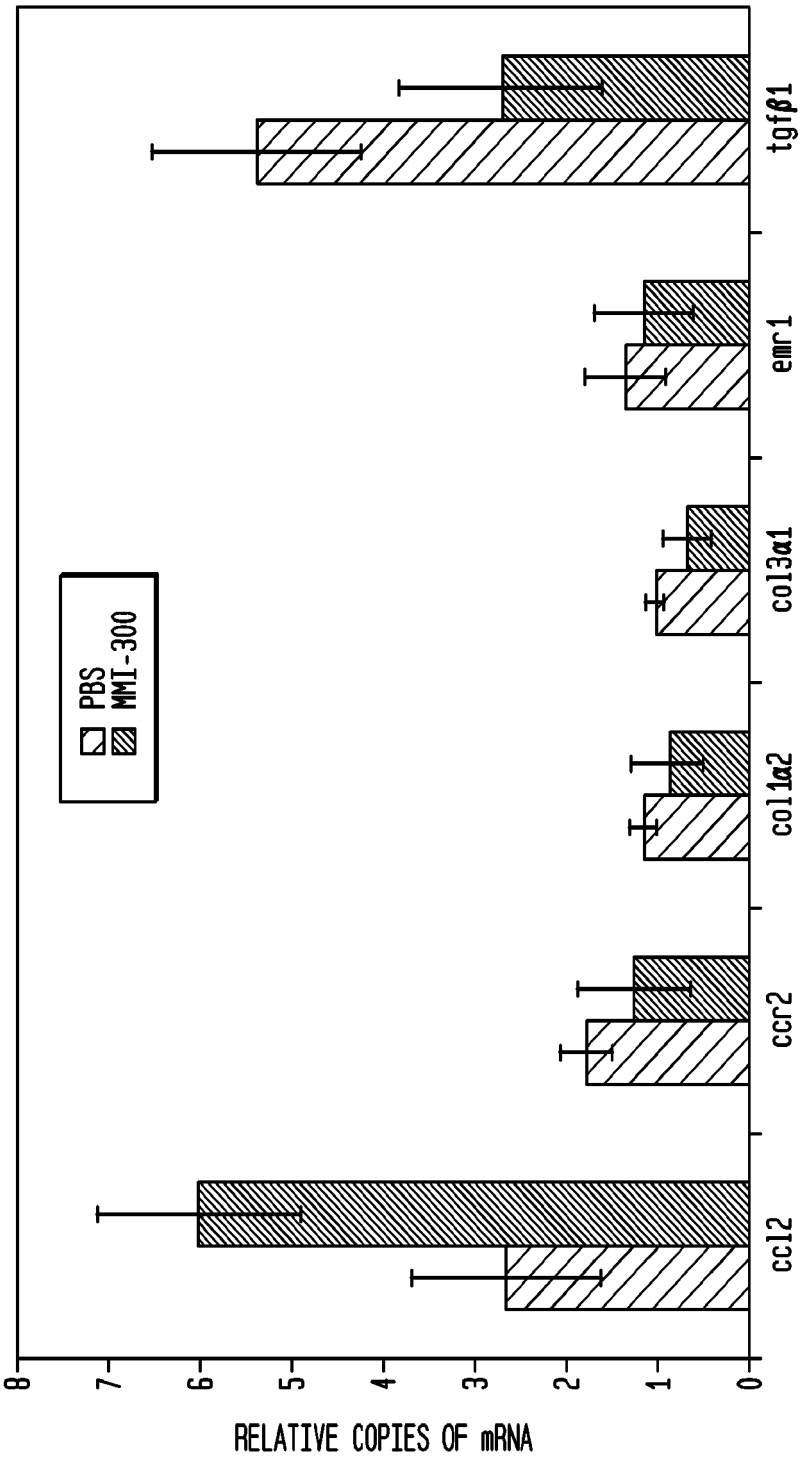


FIGURE 13

FIG. 14


PBS
MMI-300
RELATIVE COPIES OF mRNA
0
1
2
3
4
5
6
7
8
ccl2
ccr2
col1a2
col3a1
emr1
tgfβ1

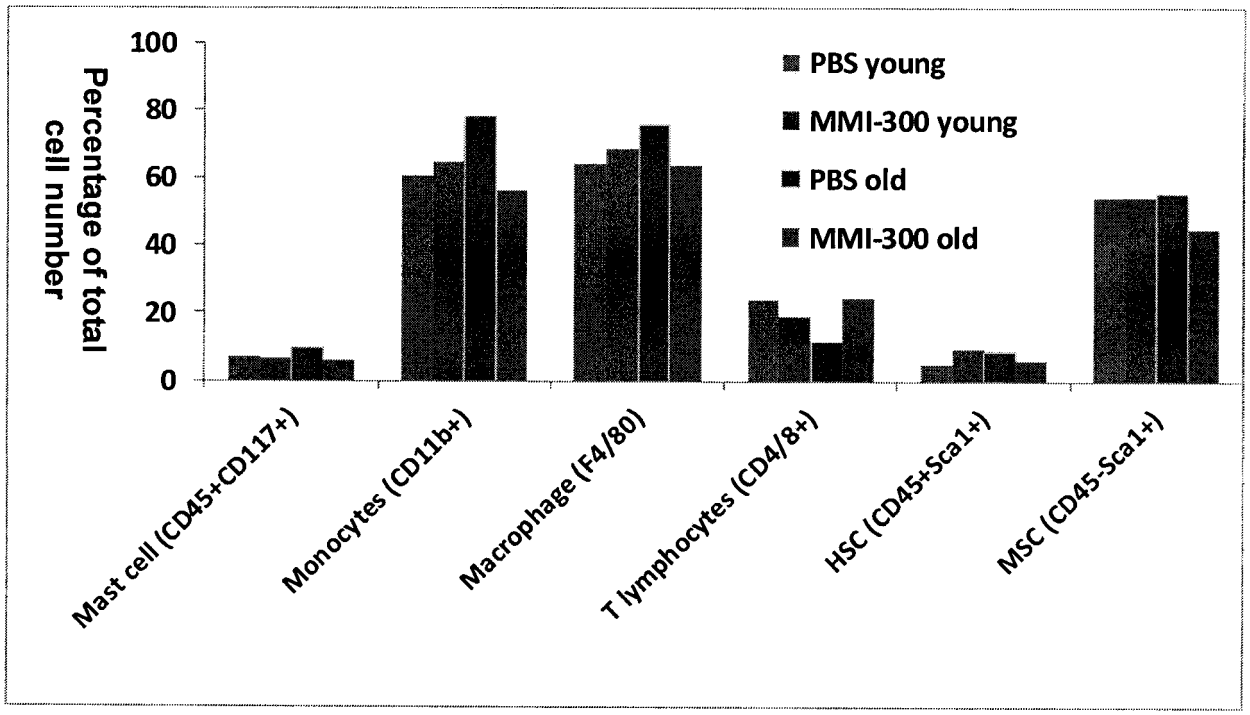

Percentage of total cell number
100
80
60
40
20
0
PBS young
MMI-300 young
PBS old
MMI-300 old
Mast cell (CD45+CD117+)
Monocytes (CD11b+)
Macrophage (F4/80)
T lymphocytes (CD4/8+)
HSC (CD45+Sca1+)
MSC (CD45-Sca1+)

FIGURE 15

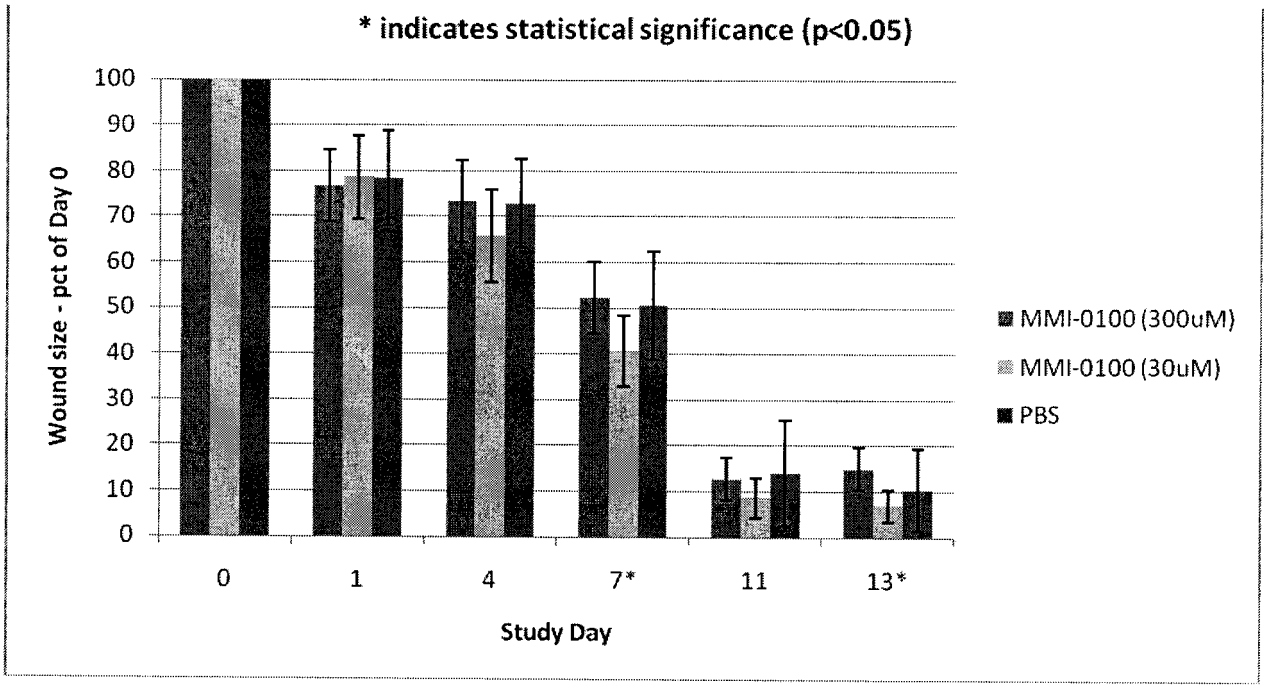

* indicates statistical significance (p<0.05)
Wound size - pct of Day 0
100
90
80
70
60
50
40
30
20
10
0
0
1
4
7*
11
13*
Study Day
MMI-0100 (300uM)
MMI-0100 (30uM)
PBS

FIGURE 16