

# Immunohistochemical Characterization of the Inflammatory Responses in Wound Healing and the Use of the Subcutaneous Polyvinyl Alcohol (PVA) Sponge Implantation Model for Evaluation of the Healing Process

Seham A Abd El-Aleem , Abir Abdelhadi Mufteh and Edward B Jude

'HSDUWPHQW RI +LVWRORJ\ 0LQLD )DFXOW\ RI 0HGLFLQH (J\SW

'HSDUWPHQW RI 3DWKRORJ\ \*DU\RXQLV 8QLYHUVLW\ /LE\D

7DPHVLGH +RVSLWDO 1+6 )RXQGDWLRQ 7UXVW DQG 7KH 8QLYHUVLW\ RI 0DQFKHVWU 8.

Corresponding author: SEG (O \$OHHP 6\$ 'HSDUWPHQW RI +LVWRORJ\ 0LQLD )DFXOW\ PHGLD, QRD, DPDM, L26 QG 7\*) EHW

Received date: \$XJXVW Accepted date: \$XJXVW Published date: \$XJXVW

Copyright: ( SEG (O \$OHHP 6\$ HW DO 7KLV LV DQ RSHQ DFFHV DUVLFOH GLVWULEXWHG XQGHU WKH XQUHVWULFWHG XVH GLVWULEXWLRQ DQG UHSURGXFWLRQ LQ DQ\ PHGLXP SURYLGHG WKH RULJLQDO D

## Abstract

**Background:** %LRORJLF DQG \IQWKHWLF ELRPDWHULDOV KDYH EHHQ XVHG IRU YDULF VWXGLHV 6XEFXWDQHRXV LPSODQWDWLRQ RI 3RO\YLQ\O \$OFRKRO 39\$ VSRQJH L VWXG\ WKH XQGHU\LQJ PHFKDQLVPV RI ZRXQG KHDOLQJ \$V D UHVHDFK WRO JUDQXODWLRQ WLVVXH IRUPDWRQ DQG WLVVXH UHJHQHUDWLRQ

**Hypothesis and Aims:** 39\$ VSRQJH PRGHO PLJKW VKRZ D GLIIHUHQW LQIODPPDWRU\ L LQFLVLRQDO ZRXQG PRGHO EHFDXVH LW UHIOHFWV WKH KRUV UHVSQRVH WR D IRU WKH LQIODPPDWRU\ UHVSQRVHV LQ WKH WZR PRGHOV

**Materials and Methods:** \$GXOW PDOH DOELQR UDWV ZHUH XVHG WR SURGXFH WKH WZR PR D PLGOLQH LQFLVLRQ WZR 39\$ VSRQJHV ZHUH LPSODQWHG VXEFXWDQHRXVO\ RQ ZHUH SURGXFHG RQ WKH GRUVXP RI HDFK UDW \$W WKH HQG RI WKH H[SHULPHQW ZHUH KDUYHVWHG DW GLIIHUHQW WLPH SRLQWV IRU DVVHVVLQJ WKH LQIODPPDW ZDV XVHG WR VWXG\ WKH FHOXODU ORFDOL]DWLRQ DQG WKH SURILOH RI WKH L :HVWHUQ EORW DQDO\VLV XVHG WR VWXG\ WKHLU SURWHLQ OHYHOV

**Results:** ,PXRKLVRFKHPLFDO VWDLQLQJ DQG :HVWHUQ EORW DQDO\VLV VKR LQIODPPDWRU\ UHVSQRVHV EHWZHHQ WKH WZR ZRXQG PRGHOV 39\$ VSRQJH LPSOD SHUVLVWHQW LQIODPPDWLRQ VWDUWHG GD\ SRVW LPSODQWDWLRQ DQG SHUVLV KDQG WKH LQFLVLRQDO ZRXQG PRGHO VKRZHG DQ HDUO\ DQG D WLPH OLPLWHG SRVW ZRXQGLQJ 0RUHRYHU WKH LQIODPPDWRU\ PHGLDWURV L126 DQG 7\*) %HWD PRGHOV :KLOH WKH VKRZHG D VLPLODU SURILOH DORQJ WKH WLPH FRXUVH LQ GLIIHUHQWLDU SURILOH LQ WKH RSHQ ZRXQG PRGHO

**Conclusion:** VXEFXWDQHRXV 39\$ VSRQJH SURYLGHV DQ LGHDO UHSURGXFWLEOH PRGHO +RZHYHU LW PD\ QRW EH D UHOLDEOH PRGHO IRU ZRXQG KHDOLQJ PRGXODWLRQ FRQLGHUDEO\ GLIIHUHQW IURP ZKDW KDSSHQV LQ WKH WLVVXHV )XUWKHUPRU GLIIHUHQWLDUO\ FRQWUROOHG E\ L126 DQG 7\*) %HWD 7KHUHIRUH DEQRUPDO ZR SKDUPDFRORJLFDO LQWHUYHQWLRQ XVLQJ QLWULF R[LGH 12 DQG 7\*) %HWD PRG

**Keywords:** :RXQG KHDOLQJ 3RO\YLQ\O DQDPPDWLRQ PPSKQJH RI ZRXQG ZRXOG LGHQWLI PHGLD, QRD, DPDM, L26 QG 7\*) EHW

\$EEUHYLDWLRQV

39\$ 3RO\YLQ\O \$OFRKRO 7\*) %HWD L126 ,QGXFWLEOH 1LWULF 2[LGH

, QWURGXFWLRQ

'LVHUVWHV RI ZRXQGV LQ WKH VNLQ SURJUHVV WKURXJK WKH VDPH HYHQWV LQ WKH WLVVXH HQG RI ZRXQG KHDOLQJ ,Q-DPPDWLRQWKH PRVW LPSRUWDQW SKDUPDFRORJLFDO UHVSQRVHV WKH LQIODPPDWLRQ KHDOLQJ > @ 8QGHUVWDQGLQJ WKH RULJLQDO UHVSQRVHV IRU ZRXQG KHDOLQJ

Citation: \$EG (O \$OHHP 6\$ 0XIWDK \$\$ -XGH (% ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
+HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
&\WRO +LVWRO

RSHQ ZRXQG LQ-DPPDWLRU UHJXODWLRQ RSHQ ZRXQG LQ-DPPDWLRU UHJXODWLRQ RSHQ ZRXQG LQ-DPPDWLRU UHJXODWLRQ  
GHSRVLWLWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
PRGHO RI ZRXQG KHDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
LQ-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
XQGHU QrupDO DQG SDWKRORJLFDQ FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ  
EH QRWHG WKLVQLWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
EHFDXVH LPSODQWDWLRQLQ-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
JUDQXODWLRQ WLWVXH IRUPDWLRQ > @ L126 DQG 7\*) % WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
KDYH EHHQ XVHG IRU YDU\LQJ PHGLFDQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
\$V D UHVDUFK WRRO 39\$ VSRQJH LV XVHG IRU YDU\LQJ PHGLFDQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
WLWVXH IRUPDWLRQ WKH FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ FRODOORJLFDQ  
DQG WLWVXH UHJXODWLRQ > @ L126 DQG 7\*) % WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
RI VWHP FHO VXYLYDO GUXJ GHOLYHU DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
,Q-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
LQFOXGLQJ QLWULF R[LGH 12 JURZWK UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
,QGXFLEOH QLWULF R[LGH V\QWKDVH L126 DQG 7\*) % WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
PDMRU PHGLDWRU RI PDFURSLQ-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
FRQGLWLRQV > @ L126 DQG 7\*) % WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
ZRXQG > @ 0RQLWRULQJ L126 DQG 7\*) % WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
XVHG DV D SDUDPHWHU IRU DVVHVVLQJ WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS

L126 DQG 7\*) % WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
PRGHO E\ VWXG\LQJLQ-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
LQ-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
GLVHUHQV\WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
DQG WKH RSHQ LQ-DPPDWLRU UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
FKRLFH RI PRGHO WKDW PLJKW EH XVHG IRU YDU\LQJ PHGLFDQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ UHJXODWLRQ  
ZRXQG KHDOLQJ

0DWHULDQV DQG 0HWKRGV

\$QLPDO

\$GXOW PDOH 6SUDJXH 'DZOH\ UDWV  
PDWFKHG SHU JURXS ZHUH KRXXVHG  
WLOO WKH HQG RI WKH H[SHULPHQW  
DOORZHGHQ RI WKH H[SHULPHQW  
FKORURIRUP RYHUGRVH +RXVLQJ DQG  
JXLGHOLQHV HVWDEOLVKHG E\ WKH  
&RPPLWWHH

39\$ 6SRQJH LPSODQWDWLRQ PRGHO

6WHULOH 39\$ VSRQJHV ZHUH SUHSDUHG  
%ULB-39\$ VSRQJHV ZLWK GLPHQVLRQV  
ORQJ ZHUH VRDNHG RYHUQLJKW LQ  
ZDWHU IRU PLQ EHIRUH LPSODQWDWLRQ  
SUHFDXWLRQV FP ORQJ LQFLVLRQ ZDV  
WKH UDW ,Q HDFK UDW IRXU 39\$ VSRQJH  
VXEFXWDQHRXV SRXFHQV GHWKURXJK  
DQG WKH VNLQHZDQV XZHJ PRQLW  
LQIHFWLRQ DW WKH RSHUDWLYH VLWH  
H[SHULPHQWV WKH 39\$ VSRQJHV ZHUH  
SRVW ZRXQGLQJ WKURXJK DQ LQFLVLRQ  
LPPXQRVWDLQLQJ RQH 39\$ VSRQJH IURP  
2SWLPDO &XWWLQJ 7HPSHUDWXUH 2&7  
VHFWLRQ IRU WKHU WKUH 39\$ VSRQJHV  
IRUFHSV WR FRODOORJLFDQ UHJXODWLRQ

SUHOLPLQDU\ H[SHULPHQW WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
VSRQJHV ZDV HQRXJK WR UXQ ZHVWHUQ EORV\WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRO 39\$ 6SRQJH ,PS  
6HFWLRQV ZHUH WKHQ LQFXEDWHG ZLWK V

Citation: \$EG (O \$OHHP 6\$ 0XIWDK \$\$ -XGH ( % ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
+HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRRO 39\$ 6SRQJH ,PS  
&\WRO +LVWRO

3DJH RI

75,7& D FRQMXJDWHG JRDW DQWL PRXVHDIURHUV\*% B&WZDZQG ZH&H FDSWXUH  
FRQMXJDWHG JRDW DQWL UDEELW IRUURP20W&ZRRXUQRPHDUKROU DW WZRRDUHDV I  
WHPSHUDWXUH 6HFWLRQV ZHUH WKHQ DZDZLQHG ZLWKH3Z&H&R&L&R&V&H&K&L&W&R&S RI  
\*HOYDWRO FRYHU VOLSSHG DQG&V&W&R&U&H&L&D&U&I&D&J&K&U&R&S&U&W&K&I&E&R&R&W&W&R&I WKH FHQW  
EHIRUH EHLQJ YLHZHG IRU DQDO\VLV 6HFWLRQHG ZHUH YLHZHG E\ /HLFD  
'05% PLFURVFRSH -R&S&R&U&H&D&W&R&E&Q&J&H&Z&Q&WK D&S&S&I&U&R&V&L&W&L&F&D&O DQDO\&V&H&V  
&O&W&H&U&W&V IRU DQDO\VLV D&Q&Q&W&E&R&R&G&I&F&D&S&W&X&H&G&Q&Z&H&U&H  
0RXVH PRQRFORQDO DQWL 7\*) EHW D&S&U&L&P&D&U&L&W&D&Q&W&L&E&R&G&L&V LV SHUIRUPHG  
5DEELW SRO\FORQDO DQWL L126 SULPD&U&L&V&Q&W&L&E&R&G&L&Z&H&U&H H&I&S&U&H&Y&D&G&R&P&W&W&K&H PHDQ  
ODERUDWRULHV \*RDW \$QWL 0RXVH 75,7& FR&Q&M&X&J&D&W&H&G V&H&F&R&Q&J&H&Q&L&W&L&E&R&G&L&V W&F&R&O  
DE \*RDW \$QWL 5DEELW ),7& FR&Q&M&X&J&D&W&H&G W&F&R&Q&J&H&Q&L&W&L&E&R&G&L&V W&F&R&O JURXS WR WKH F  
RSHQ LQM&X&U&L PRGHO RU WR WKH WZR GI  
V&X&E&F&X&W&D&Q&H&R&X&V L&P&S&O&D&Q&W&D&W&L&R&Q PRGHO Z

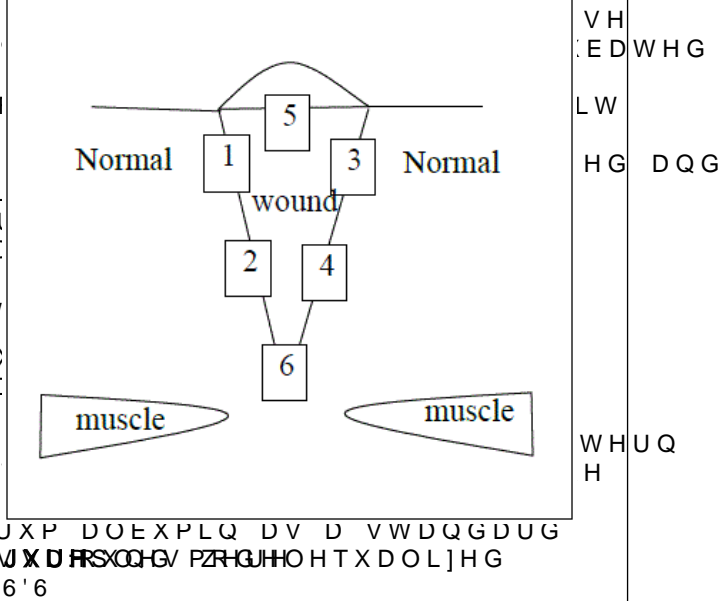
'RXEi@munofluorescence VWDLQLQJ

6HFWLRQV ZHUH SUHSDUHG DQG LQFXEDWHG ZLWK DQWLERG\ WR 7\*) %HWD  
DQWLERG\ R&Y&H&I&Q&Z&D&J&K&W&H&G&W&D&Q&G LQFXEDWHG IRU D

IXUWKHU WKLUW\ PLQXWHV ZLWK 75,7&  
VHFRQGDU\ DQWLERG\ GLOXWHG LQ 7  
ZLWK DQWLERG\ WR L126 IRU RQH  
HQ ZDVKHG DQG LQFXEDWHG ZLWK ),7& I  
VHFRQGDU\ DQWLERG\ LQ 7%6 IRU  
WHPSHUDWXUH 6HFWLRQV ZHUH PRXQW  
VWRUHG LQ OLJKW&S&U&R&R&F&V&E&L&R&G&M&G&D&Z&H&U&H YL  
'05% PLFURVFRSH -R&S&R&U&H&D&W&R&E&Q&J&H&Z&Q&WK D&S&S&I  
&O&W&H&U&W&V IRU LPDJH FDSWXULQJ DQG DQDC

+RPRJHQL]DWLRQ DQG :HVWHUQ EORW

7LVVXH V ZHUH KRPRJHQL]HG LQ D PL[W)  
PJ PO OHXSHSWLQ PJ PO SHSWD&V&W&I  
SKHQ\OPHWK\OVXOSKRQIO IXRULGH&V&H&O  
VSLQQLQJ IRU PLQ DW J WKH VXSH  
EORW D&S&U&R&W&H&L&Q FRQFHQWUDWRQ LQ  
ZRXQ&L&B&E&W&D&L&Q&H&G IURP WKH 39\$ VSRQJH  
%UDGIRUG DVVD\ > @ XVLQJ ERYLQ&H&H  
SURWHLQ FRQFHQWUDWRQV LQ&H&D&O&P&S&O&H&X&D&R&S&O&G&V P&R&H&O&H&T&X&D&O&L&]HG  
ZHUH PL[HG ZLWK&X&H&O&R&D&G&L&Q&J&+&O  
6'6



UDWLR RI DQG WKHQ BR&H&O&F&M&U&P&S&O&H&Q&Z&D&V ORDGHG  
LQ HDFK ZHOORQ D 6'SRO\DFU\ODPLGH PLQJHO %LR 5DG XVLQJ WKH  
/DHP&E&X&V&H&U&V&H&P&S&U&R&W&H&L&Q&V ZHUH W&L&P&Q&X&H&F&W&Q&W&R&X&V L&P&S&O&D&Q&W&D&W&L&R&Q&D&R&I&P&S&U&R&V  
QLWURFHOO&X&O&R&V&H P&H&P&E&U&D&Q&H&V XVLQJ D&H&W&S&R&Q&V&E&O&Z&L&W&L&Q&E&D&S&O&D&W&R&O&H&O&R&P&D&O  
H WUDQVIHU ZDV SHUIRUPHG&E&X&Y&H&U&Q&L&J&K&W&F&Y&L&R&Q&W&R&U&D&K&Y&H&U&S&V&S&R&Q&J&H L&P&S&O&D&Q&W  
P&H&W&K&D&Q&R&O JO&F&L&Q&H&I&B&Q&G&S&H&F&Z&I&F&L&O&E&I&D&O&H& W&L&P&H S&R&L&Q&W&V GD&I&V S&R&V&W L&P&S&O  
Z&D&V E&O&R&F&N&H&G E\ LQFXED&W&L&R&Q ZLWK G&E&H&F&V&F&R&O&N&S&U&R&D&P&H&L&O&D&W&R&U&Q&K&I&H&W&K&R&X&L&P&S&O  
HQ WKH P&H&P&E&U&D&Q&H Z&D&V LQFXED&W&H&G G&E&H&F&V&F&R&O&N&S&U&R&D&P&H&L&O&D&W&R&U&Q&K&I&H&W&K&R&X&L&P&S&O  
S&U&L&P&D&U&L& DQWLERG\ L126 HQ&G&D&Q&G&%&H&W&D&G&D&I&V S&R&V&W L&P&S&O&D&Q&W&D&W&L&R&Q WKH 3  
ZHUH G&H&W&H&F&W&S&O&L&P&D&O&D&I&Q&H SK&R&V&S&K&D&W&E&V&H&U&N&H&X&O&L&P&D&L&Q&E&W&K&M&D&V&R&O&D&U&E&X&H&Q&W  
3RROH 8. DQG G&H&Y&O&R&S&H&G ZL&W&D&Q&X&E&D&W&L&R&Q W&K&O&R&X&V Z&D&V&O&K&O&H&W&O&E&S&R  
L&Q&G&R&O&S&K&R&V&S&K&D&W&H Q&L&W&U&R&E&O&X&H W&H&W&S&R&I&R&O&L&Z&L&W&R&D&F&N&S&R&O&G&I&D&W&H )D&Y&X&D&H  
F&K&U&R&P&R&J&H&Q %URDG UD&Q&J&H S&U&H V&W&D&L&H&D&P&L&O&D&W&L&E&R&Q&R&D&W&K&H&U&Y&g&\$&S&R&O&D&G V&K&R&Z&H  
/D&E&R&U&D&W&R&U&L&H&V +H&P&H&O +H&P&S&V&W&H&D&G 8.L&Z&H&P&X&W&H&S&R&O&U&P&R&O&H&F&X&Q&D&Q Z&H&L&G&W S&R&V  
G&H&W&H&U&P&L&Q&D&W&L&R&Q&V & & D&Q&G&L&V&Z&D&V L&Q&G&L&F&D&W&H&G E\ WKH L&Q&F&U  
)L&J&X&U&H & D&Q&G Y&D&V&F&X&O&D&U&L&W\ )L&J&X&H H  
,P&D&J&H \$Q&D&O&V&L&V D&Q&G F&R&X&Q&W&L&Q&J RI U&P&P&X&Q&R&U&H&L&R&O&W&Y&H&X&H&O&D&G&U&D&I&P&M&K&S&U&W&H&U&G&W  
Z&R&X&Q&G&V ZL&W&P&D&F&U&R&S&K&D&J&H&V Y&S&U&G&6&O&D&D&K&S&S&R&I&G&L&H

6HFWLRQV ZHUH LPPXQRVWDLQHG ZLWK WKH F&H&O&V&L&N&H&U&V (L126 DQG 7\*)  
%HWD DQG LPDJH DQDO\VLV ZDV FDU&L&H&G&R&X&W WR H&V&W&D&E&O&L&V&K& WKH X&P&E&H&U  
S&R&V&L&W&L&Y&H&O\ V&W&D&L&Q&H&G F&H&O&O&V LQ HDFK D&Q&L&P&D&O )RU WKH 39\$ VSRQJH PRGHO F&H&O  
ZHUH F&R&X&Q&W&E&G&M&L&Q V&H&F&W&L&R&Q XVLQJ R&E&M&H&F&W&L&Y&H ; )RU WKH R&S&H&Q  
L&Q&F&L&V&L&R&Q&D&O Z&R&X&Q&G PRGHO V&H&F&W&L&R&Q V&H&F&W&L&R&Q DQDO\]HG DW ;

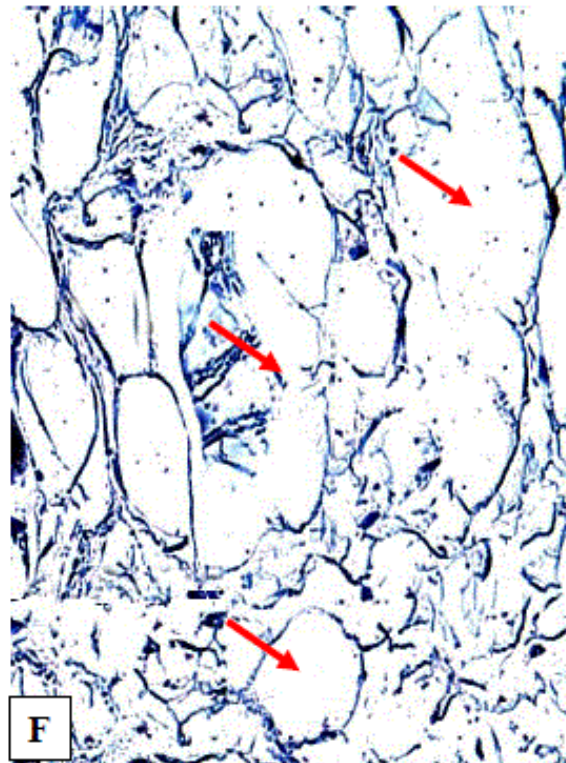
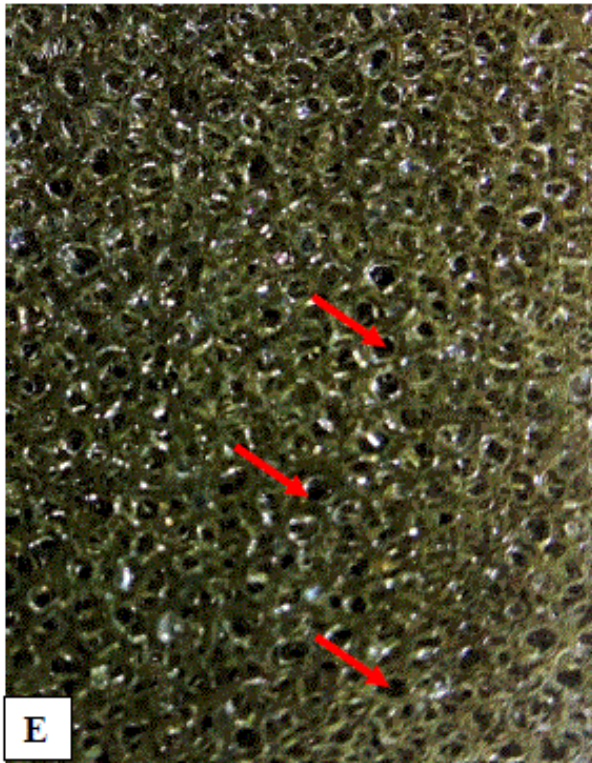
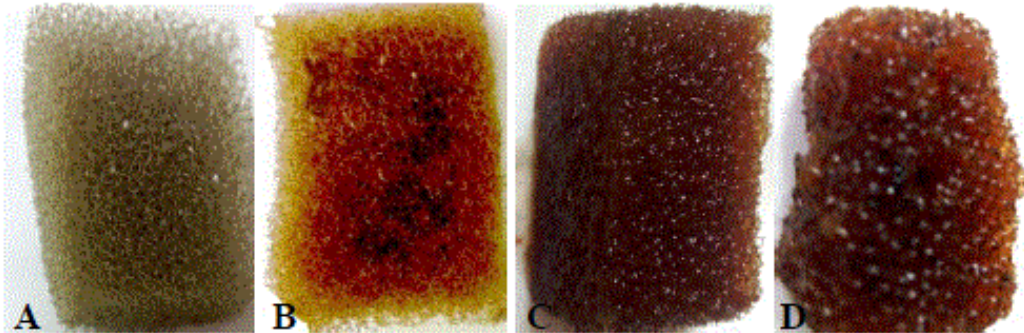
Citation: SEG (O \$OHHP 6\$ 0XIWDK \$\$ -XGH (% ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
+HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3ROI\Y\Q\O \$OFKRRO 39\$ 6SRQJH ,PS  
&\WRO +LVWRORL

3DJH RI

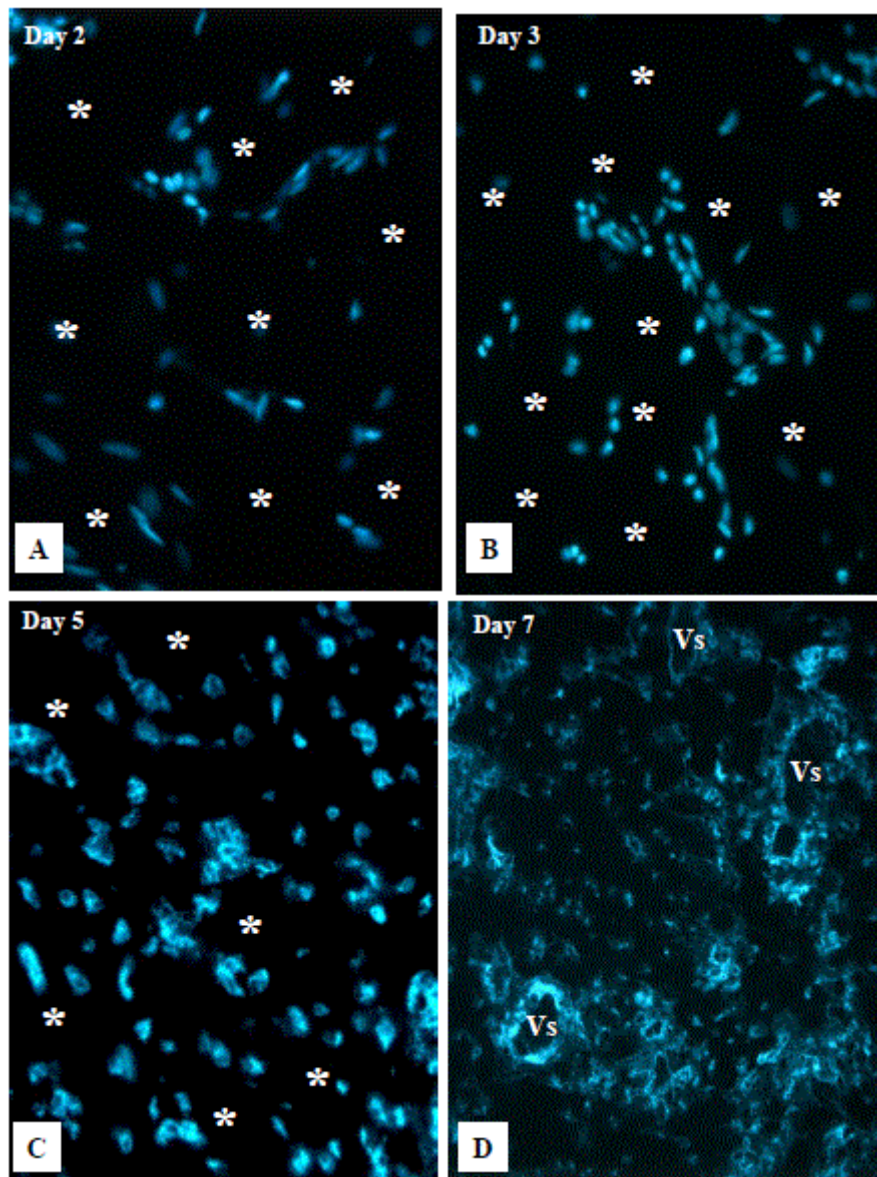
&HOOXODULW\inf\Rad\U\B\Q\B\ad\atory  
PDUNHUV LQ WKH 39\$ VSRQJH

DOO QXIF\QXIF\OHDU PDUNHU JLYHV DQ LG  
LQ\OW\ED\WL\B\G\H\W\H\U\W\SL\DW\RX\VF\W\O\O\WUHVX  
ZHUH IXUWKHU VXSIS\Q\UD\PH\O\VER\UNH\U\Q\JVXF  
W\B\RO\SR\B\JK\PD\B\H\Y\SR\QJH\Y\J\X\B\Z\H\G\D\G  
)LJXUH FHOOXODULW\ ZDV VWXGLHG E\ D QXFOHDU PDUNHU WKDW VWDLQV

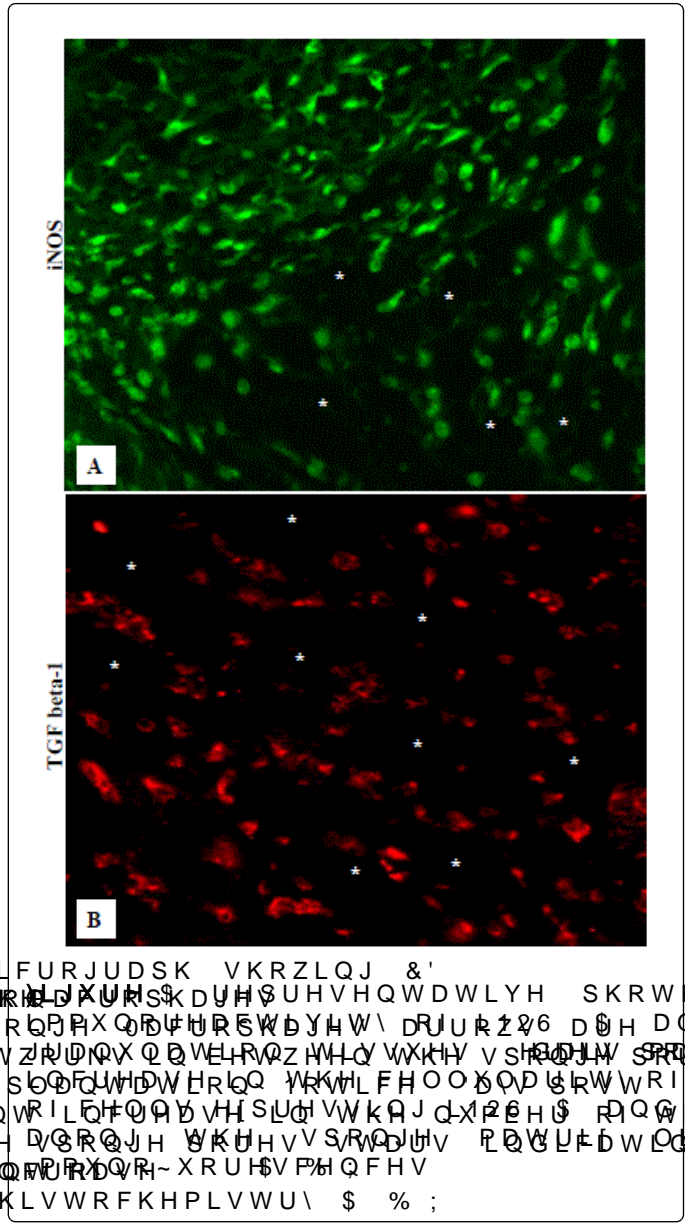
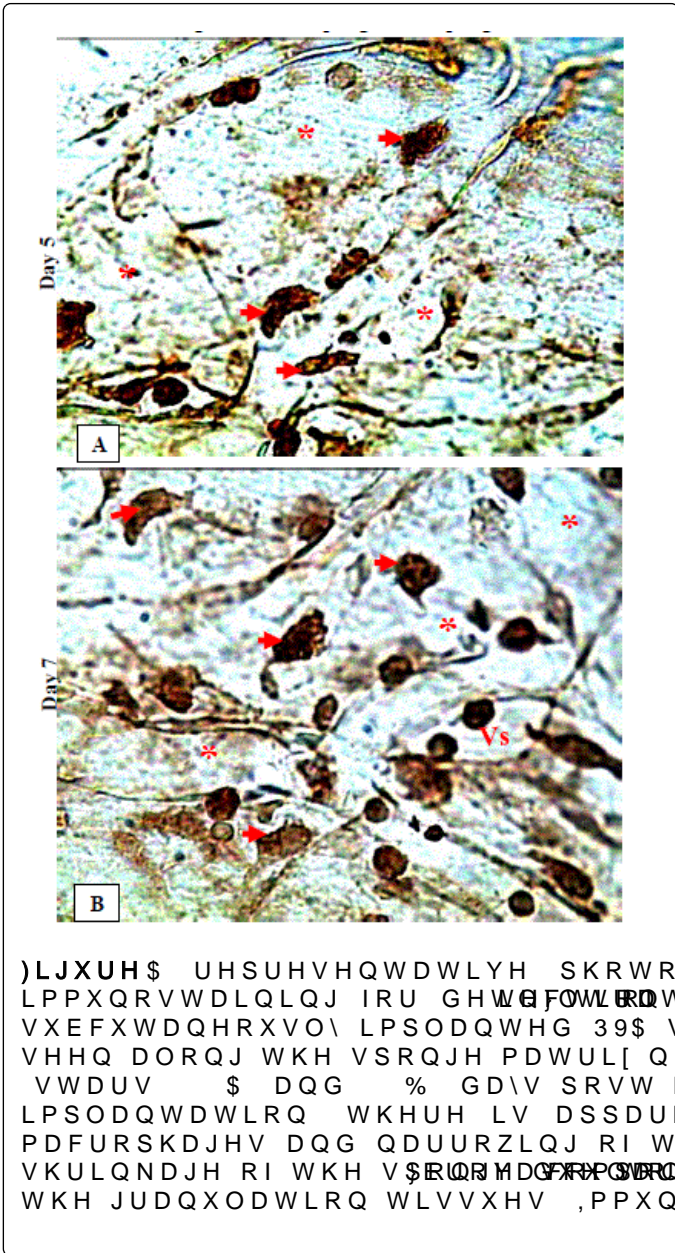
+LVWRORJLFDO H[DPLQDWLRQ RI VHF\W\B\RO\SR\B\JK\PD\B\H\Y\SR\QJH\Y\J\X\B\Z\H\G\D\G  
LQ\OW\ED\WL\B\G\H\W\H\U\W\SL\DW\RX\VF\W\O\O\WUHVX  
)LJXUH FHOOXODULW\ ZDV VWXGLHG E\ D QXFOHDU PDUNHU WKDW VWDLQV



)LJXUH FHOOXODULW\ ZDV VWXGLHG E\ D QXFOHDU PDUNHU WKDW VWDLQV  
'D\I\ SRVW LPSODQWDWLRQ VKRZLQJ WKH 39\$ VSRQJH PDFURVFRSLFD  
IXOO RI ZRXQG H[XGDWH ' 'D\I\ SRVW LPSODQWDWLRQ VKRZLQJ WKH 39\$ VSRQJH  
LQWR WKH VSRQJH SULRU WR WKH LPSODQWDWLRQ VKRZLQJ WKH SRUHV PDFURV  
DUURZV 6SRQJH LV IRUPHG RI QHWZRUN RI PDWUL\ DQG SRUHV DUURZV 7ROX

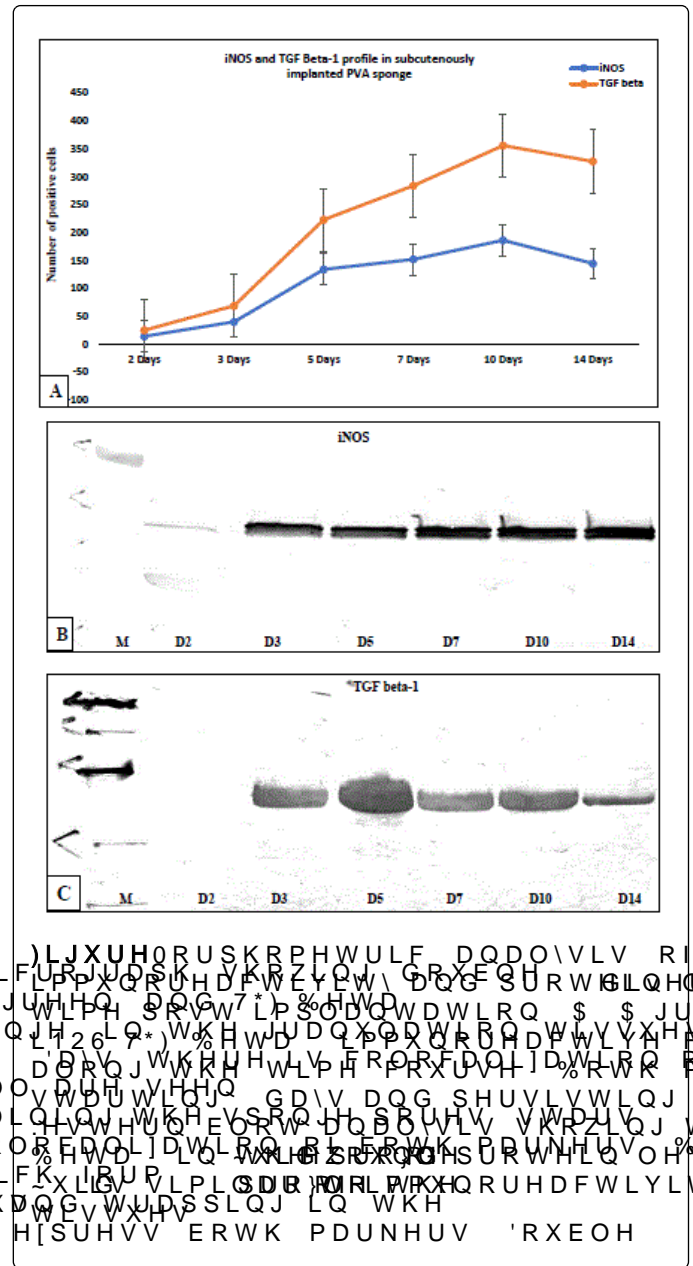
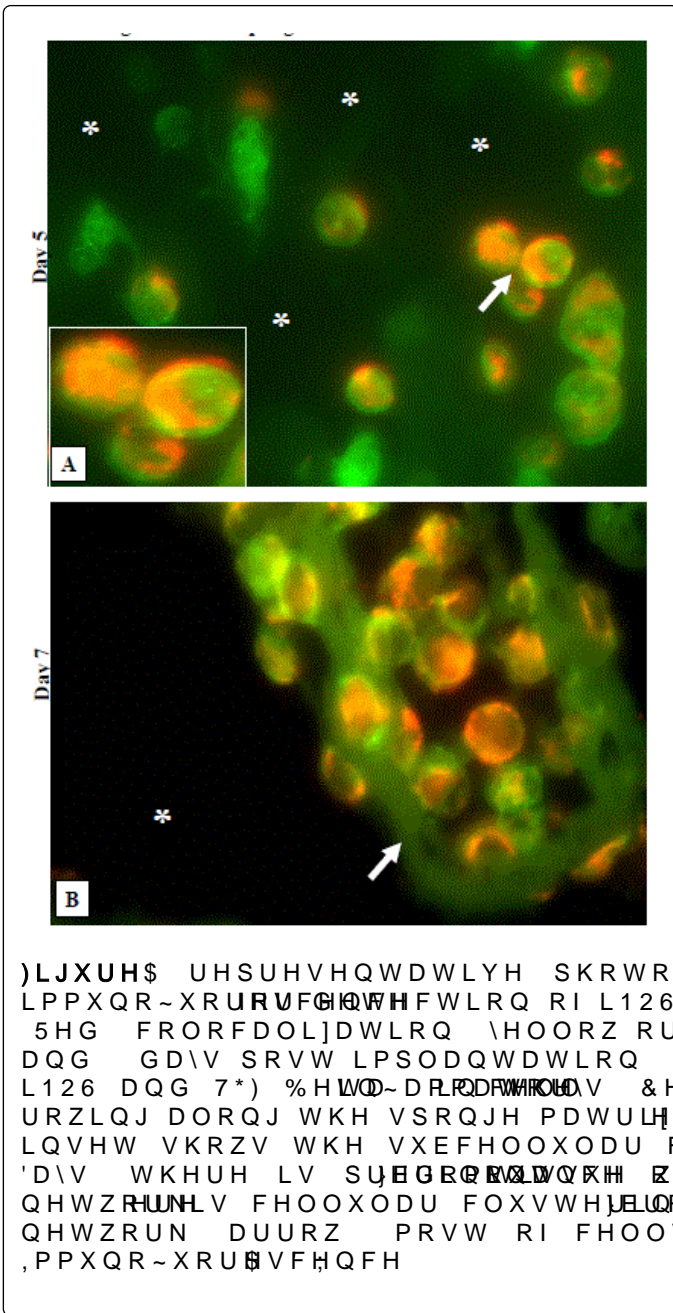


)LJXUH HUHSUHVHQWDWLYH SKRWRPLFURJUDSK VKRZLQJ +RHFVW QXFOHDU VWDL  
39\$ VSRQJH SRVW LPSODQWDWLRQ \$ 'D\ VKRZLQJ IHZ FHOOV DORQJ WKH VS  
VKRZLQJ D VOLJKW LQFUHDVH LQ WKH FHOOXODULW\ RI WKH JUDQXODWLRQ ZLV  
JUDQXODWLRQ ZLWKLQ WKH HVSRLQJ RI WKH VSRQJH FRPSRVHG RI YHVVO  
QXFOHDU VWDLQ \$ % ; & ; ' ;



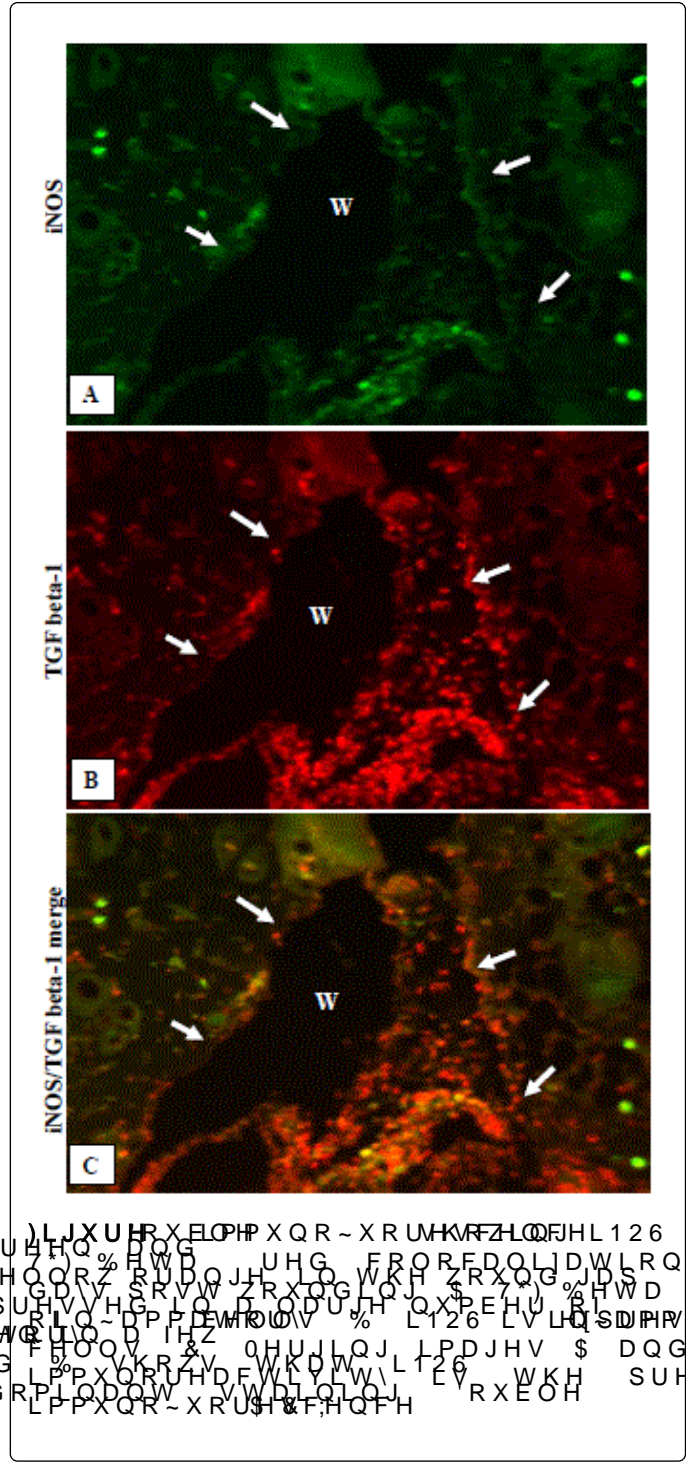
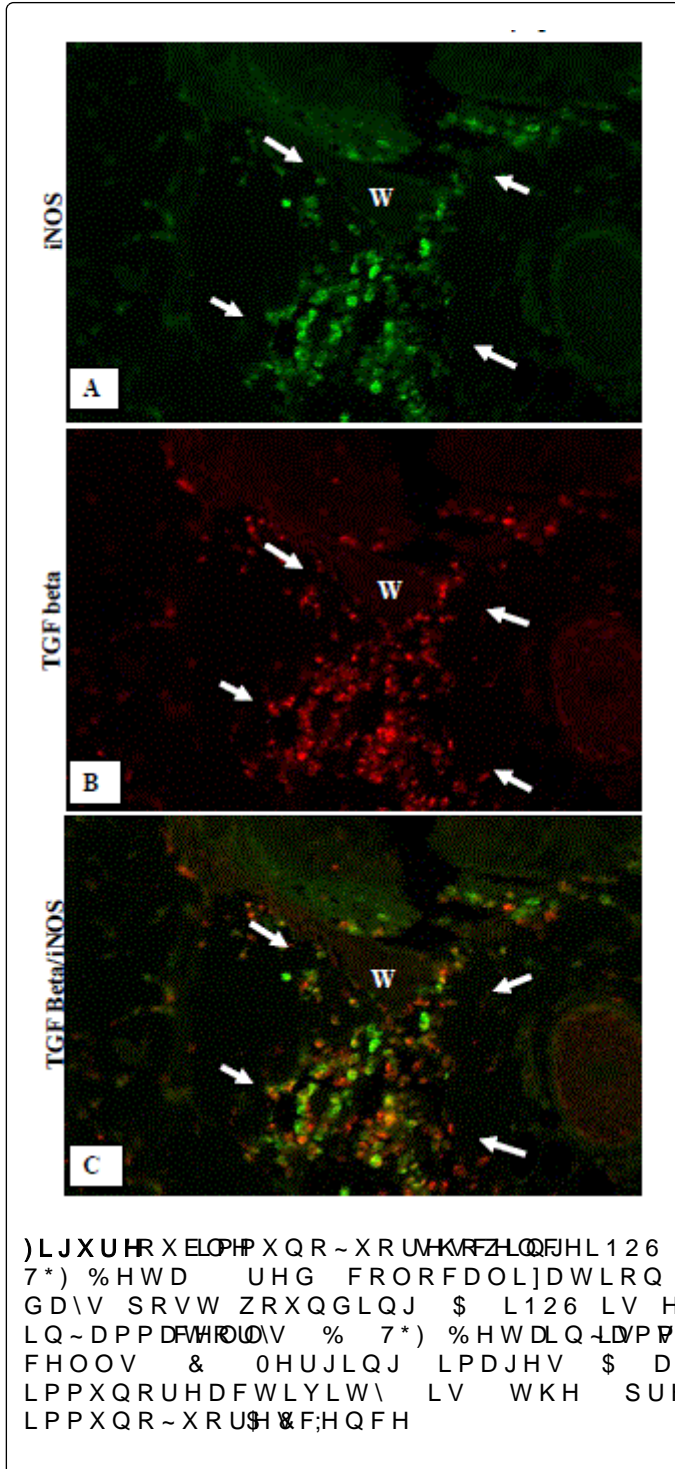
Citation: SEG (O \$OHHP 6\$ 0XIWDK \$\$ -XGH ( % ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
 +HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3ROI\YLQ\O \$OFKRRO 39\$ 6SRQJH ,PS  
 &\WRO +LVWRO

3DJH RI

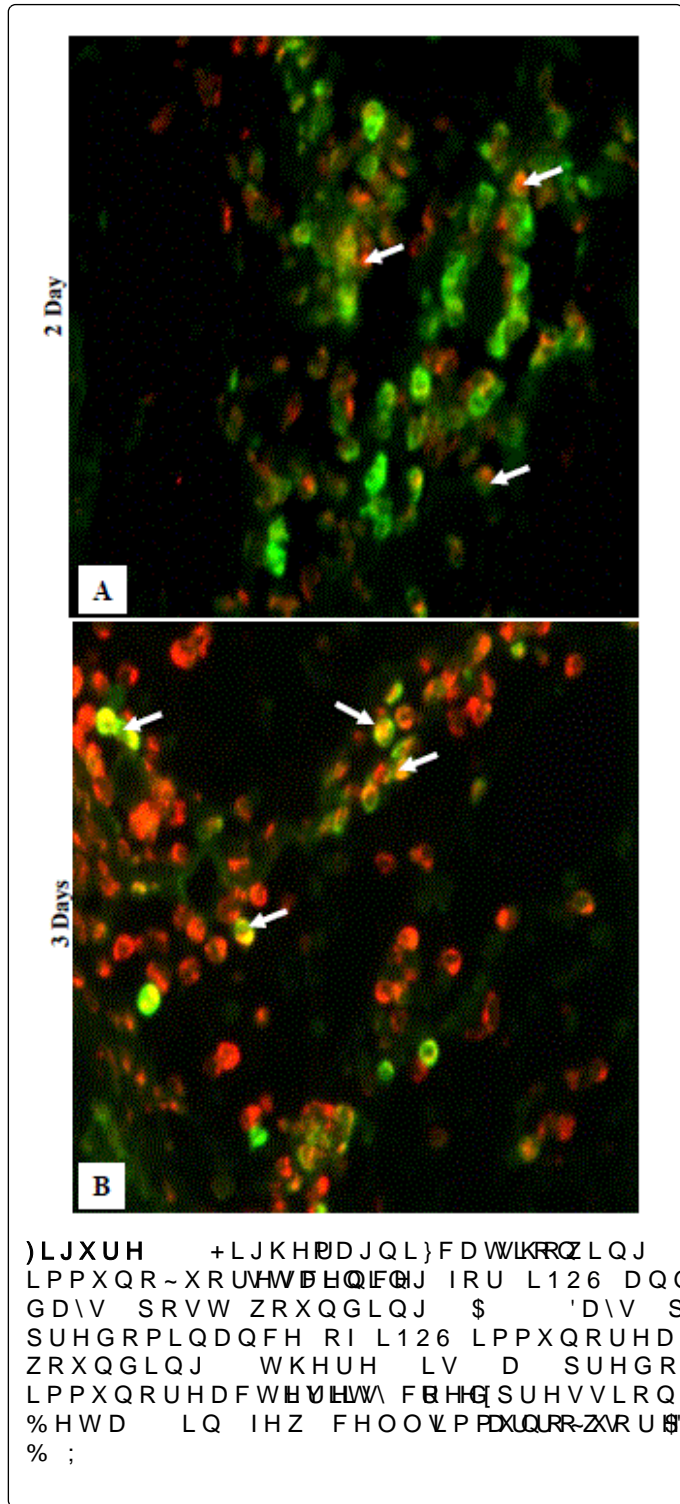


)LJXUH\$ UHSUHVHQWDWLYH SKRWRPLF LPPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
 LPPXQR~XRURVFCIWHFWLRQ RI L126 JUHQDQG 7\*) %HWD LPPXQRUHDFWLYR  
 5HG FRORFDOL]DWLRQ \HOORZ RUDQJL26 LQ\* WKH JUDQXODWLRQ \$ \$ JUDSK V  
 DQG GDIV SRVW LPSODQDWRQ \$ DROJ WKHUH WLP FRPRXUWHIWRQ PDUNH  
 L126 DQG 7\*) %HWD~DRLQDFWLRQV &HOOV ZHUH URZLQJ DORQJ WKH VSRQJH  
 URZLQJ DORQJ WKH VSRQJH PDWUL OLQVHW VKRZV WKH VXEFHOXODU FROEDQJ  
 LQVHW VKRZV WKH VXEFHOXODU FROEDQJL26 LQ\* WKH JUDQXODWLRQ \$ \$ JUDSK V  
 'DIV WKHUH LV SUBGRNOLVWKH ZKLFXLQV LPPXQRUHDFWLYR LQVHW VKRZV  
 QHWZRUN DUURZ PRVW RI FHOOV HISUHV ERWK PDUNHUV 'RXEOH  
 ,PPXQR~XRURVFCIWHFWLRQ RI L126 JUHQDQG 7\*) %HWD LPPXQRUHDFWLYR

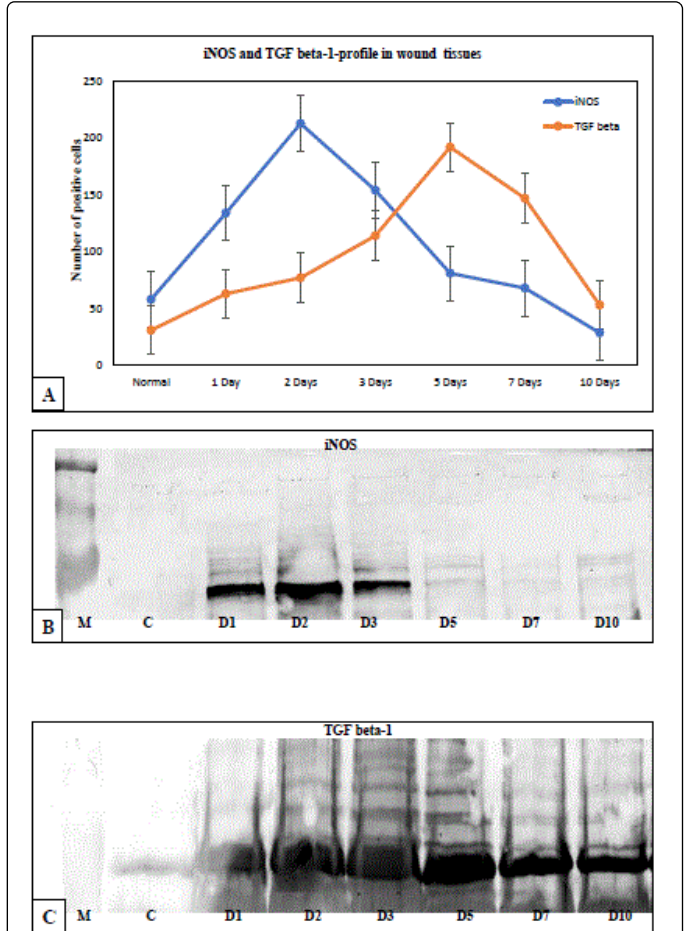
L126 DQG 7\*) %HWD LPPXQRUHDFWLYR WERPPXQRUHDFWLYR WERPPXQRUHDFWLYR  
 LPPXQR~XRURVFCIWHFWLRQ RI L126 JUHQDQG 7\*) %HWD LPPXQRUHDFWLYR  
 UHVSQRVH LQ WKH LPSODQDWRQ \$ \$ JUDSK V  
 )LJXUH \$ DQG 7\*) %HWD LPPXQRUHDFWLYR WERPPXQRUHDFWLYR WERPPXQRUHDFWLYR  
 LQ~DPPDFWLRQV ZLWKLQ WKH JUDQXODWLRQ \$ \$ JUDSK V  
 &HOOV ZHUH URZLQJ DORQJ WKH VSRQJH PDWUL OLQVHW VKRZV WKH VXEFHOXODU  
 SRUHV )LJXUH







ZHVWHUQ EORW DQDO\VLV :HVWHUQ EORW % DQG 7\*) %HWD )LJXUH & SURWHL VWDUWLQJ IURP GD\ DQG SHUVLVW W HUHIRVWKH FKDQJHV LQ WKH -DXPEDUWV H[SUHVVLRQ L126 7\*) %HWD XQDZDQFH Q SDUDOOHOHG E\ D VLPLODU FKDQJH LQ WK EORW DGGV IRXQWKH DWRGHQFH DERXW WK ERWK PDUNHUV LQ WKH 39\$ VSRQJH



)LJXUH +LJKHDDJQL}FDWKRQLQJ GRXEOH LPPXQR~XRUWPHQJ IRU L126 DQG 7\*)LJXUH DRUSKRPHWULF DQDO\VLV RI L126 GD\V SRVW ZRXQGLQJ \$ 'DIV SRVW PXPQRUHDFWLYLW\ WKLW\H DQ\ HSHWHQMHLSR LQHYW SUHGRPLQDQFH RI L126 LPPXQRUHDFWLYLW\ QGLQHH\$ %JUDSK VSRZLQJ WKH QXP ZRXQGLQJ WKHUH LV D SUHGRPLQDQFH RI L126 DQG 7\*)%HWD VKRZ D GLVWLQFW %HWD LQ IHZ FHOOLPDURZRUH VSRQJH

GRXEOH LPPXQRUHDFWLYLW\ WKLW\H DQ\ HSHWHQMHLSR LQHYW SUHGRPLQDQFH RI L126 LPPXQRUHDFWLYLW\ QGLQHH\$ %JUDSK VSRZLQJ WKH QXP ZRXQGLQJ WKHUH LV D SUHGRPLQDQFH RI L126 DQG 7\*)%HWD VKRZ D GLVWLQFW %HWD LQ IHZ FHOOLPDURZRUH VSRQJH

ORUSKRPHWULF DQDO\VLV RI WKH KLVWRORJULF DQDO\VLV RI WKH VSRQJH HUHZDV D JUDGXDO LQFUHDVH LQ WKH L126 DQG 7\*)LJXUH DRUSKRPHWULF DQDO\VLV RI L126 LPPXQRUHDFWLYLW\ RYHU D WLPH FRXUVH 7DEOH 6WDUWLQJ WKUHH GD\V SRVW LPSODQWDWLRQ DQG FRQLQXHG WR LQFUHDVH XS WR GD\V SRVW LPSODQWDWLRQ )LJXUH \$RQ\PHQWKMLQJDO\ WKLV ZDV

ORUSKRPHWULF DQDO\VLV RI WKH KLVWRORJULF DQDO\VLV RI WKH VSRQJH HUHZDV D JUDGXDO LQFUHDVH LQ WKH L126 DQG 7\*)LJXUH DRUSKRPHWULF DQDO\VLV RI L126 LPPXQRUHDFWLYLW\ RYHU D WLPH FRXUVH 7DEOH 6WDUWLQJ WKUHH GD\V SRVW LPSODQWDWLRQ DQG FRQLQXHG WR LQFUHDVH XS WR GD\V SRVW LPSODQWDWLRQ )LJXUH \$RQ\PHQWKMLQJDO\ WKLV ZDV

Citation: SEG (O \$OHHP 6\$ 0XIWDK \$\$ -XGH (% ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
 +HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQ\O \$OFKRRO 39\$ 6SRQJH ,PS  
 &\WRO +LVWRO

3DJH RI

L126 DQG 7\*) %HWD H[SUHVVLQR LQ ZRXXQGLQJ WKH QNHUHVW  
 ZRXXQGLQJ WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 ,PPXQR~XRUVW DQWJ VKRZHG L126 DQG 7\*) %HWD WKH QNHUHVW  
 LPPXQRUHDFWLYLW\ DW WKH ZRXXQGLQJ WKH QNHUHVW WKH QNHUHVW  
 DW HDUO\ WLPH SRLQWV GD\ )LJXU\ WKH QNHUHVW WKH QNHUHVW  
 ZRXXQGLQJ LPPXQRUHDFWLYLWLV ZHUH PRUSKRPHWULFDQ\ DQDQVHG  
 E\ FRXQWLQJ WKH QXPEHU RI FHOOV H[SUHVVLQR L126 DQG 7\*) %HWD  
 GLVHULQW SRVW ZRXXQGLQJ WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 DQG 7\*) %HWD DW HDUO\ WLPH SRLQWV E\ FRPSDULVRQ WKH FRQWUROV

Groups	iNOS	P Value	TGF Beta-1	P Value
'D\ 3RVW LPSODQWDWLRQ	"		"	
'D\ 3RVW LPSODQWDWLRQ	"	3	"	3
'D\ 3RVW LPSODQWDWLRQ	"	3	"	3
'D\ 3RVW LPSODQWDWLRQ	"	3	"	3
'D\ 3RVW LPSODQWDWLRQ	"	3	"	3
'D\ 3RVW LPSODQWDWLRQ	"	3	"	3

5HDGLQJV UHSUHVHQW WKH DYHUDJH QXPEHU RI SRVLWLYH FHOOV DW HDFK WLPH SRLQW  
 5HVXOWV DUH H[SUHVHG DV WKH PHDQ ± 6(0 3 YDOXH 3 3

7DEOH 1 KDQJHV LQ WKH OHYHOV RI L126 DQG 7\*) %HWD LPPXQRUHDFWLYLWLV  
 LPSODQWLVWKH QNHUHVW SRLQWV

Groups	iNOS	P Value	TGF Beta-1	P Value
&RQWURO	"		"	
'D\ SRVW ZRXXQGLQJ	"	3	"	3
'D\ SRVW ZRXXQGLQJ	"	3	"	3
'D\ SRVW ZRXXQGLQJ	"	3	"	3
'D\ SRVW ZRXXQGLQJ	"	3	"	3
'D\ SRVW ZRXXQGLQJ	"	3	"	3

5HDGLQJV UHSUHVHQW WKH DYHUDJH QXPEHU RI SRVLWLYH FHOOV FRXQWHG LQ WKH ZRXXQGLQJ DV WKH  
 3 3

7DEOH 2 KDQJHV LQ WKH OHYHOV RI ZRXXQGLQJ L126 DQG 7\*) %HWD LPPXQRUHDFWLYLWLV

'LVFXVVLQR SDUDFULQH SURGXFWLRQ RI PHGLDWRUV V  
 ,Q WKLV VWXG\ ZH KDYH VKRZQ WKDW L126 DQG 7\*) %HWD WKH QNHUHVW  
 GLVWLQFW SDUDFULQH SURGXFWLRQ WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 LQFLVLRQDO GHUPDO ZRXXQGLQJ WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 L126 DQG 7\*) %HWD L126 DQG 7\*) %HWD WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 PRGHQV :KLOH LQ WKH 39\$ VSRQJH L126 DQG 7\*) %HWD WKH QNHUHVW  
 DV ORQJ DV WKH 39\$ VSRQJH H[LVWV LQ WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 KDYH WLPH OLPLWHG H[SUHVVLQR 2XU ELRROZDFXQDV DQGHURWZLQK DSKHYLROV  
 VWXGLHV HUIHQWKH 39\$ VSRQJH LPSODQWLVWKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 LQ~DPPDQWIRU DV ORQJ DV WKH LQ~DPPDQWIRU WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 UHDFWLRQ WR DXVRWKILJQPRGHQ FDQ XEFXFWLRQ SURGXFWLRQ RI YDVRDFWLY  
 LQ~DPPDQWIRU UDWKHU WKDQ D ZRXXQGLQJ WKH QNHUHVW WKH QNHUHVW WKH QNHUHVW  
 PXOWLSKDVH ZLWK WLPH OLPLW > @ ORUHYHU FURSKUH DSKORFDWRYDQV

Citation: \$EG (O \$OHHP 6\$ 0XIWDK \$\$ -XGH ( % ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
+HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQIO \$OFKRRO 39\$ 6SRQJH ,PS  
&\WRO +LVWRO

GHDG FHOOV +RZHYHU WKH\ DUH XQD)XOHV KRU BRUHVVM 2WR ERDWSOJWV ZORXOG ID  
VHULHV RI HYHQWV FRXOGLDFRPOZWLWRO WUKMLSRQNDQWVWVWROQ HIRWKH SUHGRPLQD  
FRQWLQXR XV SURGXFWLRQ RI L126 DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
H HDUO\ XSUHJXODWLRQ RI L126 DQG F\WRWRIF HQYLURQPHQW WKURXJK  
LQ-DPPDWRUHOV DQG FRORFDOL]DWLRQ DQWLHWRWKH PDUNXUV SURYLG  
HYLGHQFH WKDW WKH\ ZHUH H[SUHVVHG DV D SRDUV RI WKH LOWHJUDWVHGH UHYSR  
WRQ-DPPDWRUHOV )DFWRUV DYDLODEOH ZKLFK ERXOG LOWHJUDWVHGH UHYSR  
OLSRRO\VDFFKDULGHV /36 DQG F\WRWRIF DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
DQG 7\*) %HWD VLPXOWLPXU\ L126 @LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
%HWD XSUHJXODWLRQ ZDVLOR DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
ZRXQGLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
F\WRNLQHV ZKLFK DUH XVXDOLQ-DPPDWRUHOV )DFWRUV DYDLODEOH ZKLFK ERXOG  
SKDVH > @ )ROORZLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
LQYDVLRLQ UHOHDVH RI EDFWHULDO OLSRSRO\VDFFKDULGHV UHYSR  
L126 V\QWKHVLV LQ WKH QHXWURSKLOV DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
> @ 12 KDV DQWLPLFURELDO DQG DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
)XUWKHUPRUH 12 PBRQZWLQWKHE OLSRSRO\VDFFKDULGHV UHYSR  
IDFLOLWDLQJ QXVWUWDLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
XSUHJXODWHG L126 LQFUHDVH 12 SURXVLRQV RI RYHUFRPH WKH F\WRWRIF  
HQYLURQPHQW WKURXJK DQWLPLFURELDOV YDVBGLDQWDLRQ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
DJJUHJDWLRQ DFWLYLWLHYEVRJHWRN\KPHWLDJ YHVDUFK )LUVWO\ 39\$ VSRQJH  
> @ LWV XSUHJXODWLRQ SRVWLQMXU\ UHSDLU DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
JURZWK DQG UHSDLU DV LW LV HVVHQWDO WR LQWHUURJLQJ SURJUDPPDWLRQ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
GLVHUHQV SURWHLQ DQG FROODJHQ V\QWKHVLV LQ WKH 39\$ VSRQJH PRGHO DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
UHTXLUPHQWV IRU FRPSOHWLRQ RI WKH 39\$ VSRQJH PRGHO DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
WR RYHUFRPH WKH F\WRWRIF HQYLURQPHQW DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
WR SURPRWH SRVWLQMXU\ UHSDLU DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
LQMXU\ +RZHYHU L126 DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
H[SUHVVLRQ LQ WKH RSHQ ZRXQG PRGHO LV SRVVLEOH WR ZRUJWK GLVXVVLQJ LQ  
IXUWKHU GHWDLOV  
DEQRUPDO KHDOLQJ /RZ 12 SURGXFWLRQ  
,QWHUHVWLQJO\ ZH KDYH VKRZQ D GLVWLPDQVSRQVHDEH WYH 126 DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
EHWD UHJXODWLRQ LQ WKH RSHQ LQVXVWDLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
H[SUHVVLRQ SUHGRPLQDWHG WKH ZRXQG FRQWUROV SURGXFWLRQV DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
ZRXQGLQJ 7\*) %HWD SUHGRPLQDWHG ZRXQG FRQWUROV SURGXFWLRQV DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
FRXOG EH H[SODLQHG E\ D QXPEHU RI ZRXQG KHDOLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
L126 LV SURGXFWHG E\ QXVWUWDLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
LQWR WKH ZRXQG DQG SURJUDPPDWLRQV DW @DUO\ SKDVH  
ORUHRYHU QHXWURSKLOV SURGXFW F\WRNLQHV WKDW LQGXFH L126 > @  
2Q WKH RWKHU KDQG 7\*) %HWD LV SURGXFWHG E\ PDFURSKDJHV  
)EUREDQWV DV EUREDQWV DW D ODWHU SKDVH RI :RXQG KHDOLQJ DLPLQJ IRU  
LQ-DPPDWRUHOV 6HFRQGDULO\ WKH ZRXQG ELRFKHPLFDO  
HQYLURQPHQW LQWKH DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
FRQFHSW 7\*) %HWD SURGXFWLRQ LQ WKH ZRXQG @LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
DQG LQGXFHV PHGLWRUV VXFK DV DUJLQDVH > @ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
> @ ZKLFK LQKLELWGO\ WRUH@XODWLRQV DW @DUO\ SKDVH  
SURGXFW 12 ZKLFK FRPELQHV ZLWK K\GULYHUVH UDG LFDQV RYHU KHDOLQJ PH  
SHUR\QLWULWH > @ ZKLFK DORQJ ZLWK SVXSHU[LGH DQG RWKHU WR[LF IUHH  
UDGLFDQV FDXVHW OHQV @DLQHDG@WR WKH K\GULYHUVH UDG LFDQV RYHU KHDOLQJ PH  
DUJLQDVH ZLWKLQ WKH H[WUDFHOOXODQV DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
WKURXJK FRPSHWLWLRQ IRU / DUJLQDVH V\QWKHVLV LQ @PXLQV DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
GLVHUHQV SURWHLQ RI L126 DQG 7\*) %HWD LQ WKH RSHQ LQMXU\  
PRGHO LV UHJXODWHG E\ WKH ZRXQG FHOORZWLQJ W\ JRZQXGLDQWDLRQ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
ZRXQG ELRFKHPLVWU\  
SRO\HWKHU SRO\UHWDQH VSRQJH LPSODQ  
KLVWRSDWKRORJ\  
H SDWWHUQ RI H[SUHVVLRQ RI L126 DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
ZRXQG FRXOG EH D SK\VLORJLFDO UHTXLUHQW LQRUQKHDOLQJ DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
SRVWLQMXU\ WKH ZRXQG HQYLURQPHQW LV FKHPLVWULYH ZLWK 5E DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
> @H UHOHDVH RI EDFWHULDO OLSRSRO\VDFFKDULGHV UHYSR  
L126 V\QWKHVLV LQ WKH QHXWURSKLOV DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX  
> @ 12 KDV DQWLPLFURELDO DQG DQWLPLFURELDO DQGL726 %LQWVKH HDUO\ VWDJH LQFUHDVH ZRX

Citation: \$EG (O \$OHHP 6\$ OXIWDK \$\$ -XGH ( % ,PPXQRKLVWRFKHPLFDO &KDUDFWHUL] +HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3ROI\YLQIO \$OFRKRO 39\$ 6SRQJH ,PS &\WRO +LVWRO

3DJH RI

%DUFHORV 3URGXFWLRQ...  
& / . & DQG & / - ( LQQD...  
PLFH - DPPD...  
%HOR \$...  
VXEFXWDQHRXV WXP...  
2 EULHQ...  
0DWHULDOV WRGD...  
-LDQJ ; ;LDQJ 1 =KDQJ + 6XQ < /LQ = H...  
FKDUDFWHUL]DWLRQ RI SRO\ YLQIO DQFRK...  
KLJK WRXJKQHV DQG HOHFWULF FRQGXFWER...  
6FKI... 1LWULF R[LGH PHWDEROLVP...  
%URZQ ' / .DR :: \*UHHQKDOJK ' \*...  
LQ-DPPD...  
SDWVHUQV LQ GLDEHWHV DQG LPSURYH...  
6XUJHU \...  
6LQJHU \$- &ODUN 5\$ &XWDQHRXV ZRX...  
MRXUQDO RI PHGLFLQH...  
ODFKDGR 5' 6DQWRV 5\$ \$QGUDGH 63...  
DQJLRWHQV LQV RQ DQJLRJHQHV LV /LH...  
)HUHULUD 0\$ 6SRQJH\_LQG...  
3\$) UHFHSWRU...  
SKDUPDFRORJ\...  
\*DEELDQL H P\R}EURE...  
)EURFRQ...  
3DWKRORJLFDO 6RFLHW\ RI \*UHDW %ULWDLQ...  
'DYLGRQ - \$QLPDO PRGHV IRU ZRX...  
GHUPDWRORJLFDO UHVHDFK... 6 6...  
<DQ...  
SHULSKHUDO QHUYHV UHTXLUHV FRQWURO...  
IRUPDWLRQ :RXQG 5HSDLU DQG 5HJHQH...  
)DOVK ' ,QQHUYDWLRQ DQG QHXURN...  
DQJLRJHQHV LV LQ WKH...  
)RUG +5 &KDUDFWHUL]DWLRQ RI ZRX...  
PDWUL PRGO \$UFKLYHV RI 6XUJHU \...  
(IURQ %DUEXO \$ 6XEFXWDQHRXV VSR...  
+HDOLQJ 6SULQJHU SS -RXUQDO RI 3DWKRORJ\...  
'HVNLQV\$UGHVWDQL 6 <RX...  
PRGO LPSODQDWLRQ -RXUQDO RI YLVX...  
5RPSHQ H HV...  
WRSRJDSK\ DQG RI LPSODQW FR...  
LQWHJUDWRQ D OLWHDWXUH UHYLZ &...  
OF1DOO\ \$ . 9LWURQHFWLQ LV D...  
,/\_LQGXFHG IRUHLQJ ERG\ JLDQW FHOO...  
0DWHULDOV 5HVHDFK 3DUW \$...  
)LH 'XDO JURZWK IDFWRU...  
ZRXQG KHDOLQJ \$FWD ELRPDWHULDOLD...  
)OD...  
&RPSDULWRQ RI WKH SROI\YLQIO DQFRK...  
SROI\WHWUD-XR...  
ZRXQG KHDOLQJ SRWHQWLDLQ LQ XPDQ...  
5HJHQH...  
6SUXJHO (VHF...  
SRURXV VXEFXWD...  
\*DUODQG &- 0F3KHUVRQ \*\$ (YLGHQFH...  
PHGLDWH WKH KISHUSRODUL]DWLRQ DQG...  
VPOO PHVHQWHULF DUWHU \ %ULWLVK MRX...  
%UDLPDQ :LVNPDQRYHO LQVLJKW LQWR...  
RI HYHQWV 7R[LFRORJLF SDWKORR...  
)XR- ' &KHQ \$) 1LWULF R[LGH D QHO...  
ZRXQG KHDOLQJ \$FWD 3KDUPDFRORJLF...  
&KDQJ & , /LDR -& .XR /...  
SURGXFWLRQ LQ DFWLYDWHG PDFURSKDJHV...  
+HDUW DQG &LUFXODWRU\ 3K\VLRO...  
6KDK 0 )RUHPDQ ' 0 )HUXVRQ 0...  
6KDK 0 5ROH RI HOHYDWHG...  
PHGLDWH VLW...  
VPDOO PHVHQWHULF DUWHU \ %ULWLVK MRX...  
%UDLPDQ :LVNPDQRYHO LQVLJKW LQWR...  
RI HYHQWV 7R[LFRORJLF SDWKORR...  
)XR- ' &KHQ \$) 1LWULF R[LGH D QHO...  
ZRXQG KHDOLQJ \$FWD 3KDUPDFRORJLF...  
&KDQJ & , /LDR -& .XR /...  
SURGXFWLRQ LQ DFWLYDWHG PDFURSKDJHV...  
+HDUW DQG &LUFXODWRU\ 3K\VLRO...  
6KDK 0 )RUHPDQ ' 0 )HUXVRQ 0...  
6KDK 0 5ROH RI HOHYDWHG...  
PHGLDWH VLW...  
VPDOO PHVHQWHULF DUWHU \ %ULWLVK MRX...  
%UDLPDQ :LVNPDQRYHO LQVLJKW LQWR...  
RI HYHQWV 7R[LFRORJLF SDWKORR...  
)XR- ' &KHQ \$) 1LWULF R[LGH D QHO...  
ZRXQG KHDOLQJ \$FWD 3KDUPDFRORJLF...  
&KDQJ & , /LDR -& .XR /...  
SURGXFWLRQ LQ DFWLYDWHG PDFURSKDJHV...  
+HDUW DQG &LUFXODWRU\ 3K\VLRO...

Citation: SEG (O \$OHHP 6\$ OXIWDK \$\$ -XGH (% ,PPXQRKLVWRFKHPLFDO &KDUDFWHULJ  
+HDOLQJ DQG WKH 8VH RI WKH 6XEFXWDQHRXV 3RO\YLQ\O \$OFKRO 39\$ 6SRQJH ,PS  
&\WRO +LVWRO

3DJH RI

&DVVDW\$OOD ,QWHUOHXNLQ\_ SURGXFWLQJH WELKXSSRVLWH UHJXODWLRQ RI SUR  
SRO\PRUSKRQXFOH DU OHXNRF\WHV (XURSHDQDQXLRQDQJLIDRQZKQIWDJWGRHXNLQ LQ D  
-XGH ( 7UDQVIRUPLQJ JURZWK IDFWRU\_XHOMXUHV -RQDQDQFHSVRIKWRSPXQRORJ\  
DQG ,, LQ GLDEHWLF IRRW XOFHUV 'LDEHWLFDOHQGLFLQKOG \$ \$UJLQLQH PHWDEROLY  
(SOHHP 6\$ \$EGHOZDKDE 6 2VPDQ 1 VLFHQSHUHXOHWLZRQDQ +HDOLQJ 6RXWKHUQ  
WUDQVIRUPLQJ JURZWK IDFWRU EHWD DQG%QHFWDDQ R]BGH V\QWSSDHLQWHHQRGLR]EO U  
FRPSDULVRQ WR QRUPDO KXPDO DQDQDQSRSDUHQWLRQHWHRULPSOLFDFWLRQV IRU HQGRW  
SDWKRJHQHVLV RI NHORLG - &\WRO +LVWROVXSHUR[LGH 3URF 1DWO \$FDG 6FL 86\$  
9RGRYRW] 5HJXODWLRQ RI WUDQVIRUPLQJHOBWRYREVRQ ' .XOLN 7- 1LWULF  
R[LGH &DQFHU UHVHDFK FRPSRXQGV LQKLELW WRWDO SURWHLQ DQ  
%RXWQUG 7UDQVIRUPLQJ JURZWK IDFWRU\_YHWFDOVLYRORWKPXVJQHDXH FOH FHOV  
DFWLYLW\ LQ PDFURSKDJHV ,PSOLFDFWLRQV&DRU OWKIHVWHHJKODKWHHQ/DUVRDF\$RSIKDJEL]L &  
F\WRWRHLFLXUQDO RI ,PPXQRORJ\ +S HW DO 1LWULF R[LGH LQKLELWV W  
&RUUDOLJD \$UJLQDVH LQGXFWRQ E\ VXS\$UWKRWV DQWHUWULF&RQSH P51\$ DEXQGDQ  
V\QWKHVLV ,/ ,/ DQG 3\*( LQ PXULQAREKHOPIWDRZHGHU%LRKHPLFDO -RXUQDO  
PDFURSKDJHV %LRFKHPLFDO DQG ELRSK\VRDQVHDFKJHFRUFDFQDFDQWVREWRORS\$DQ  
2[IRUG 8QLYHUVLW\ 3UHVV