FIGURE 1

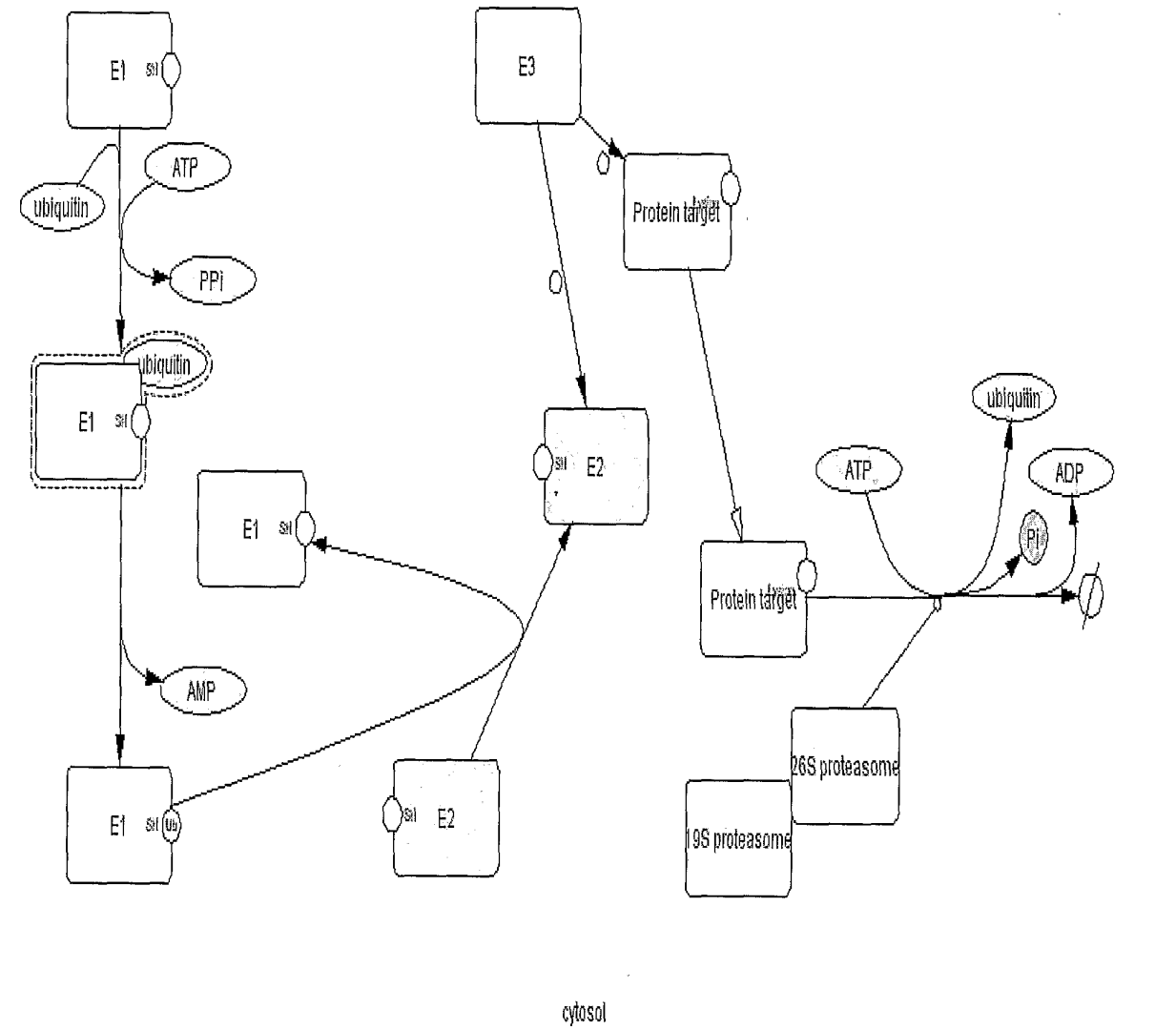

E1
E3
ATP
ubiquitin
PPi
Protein target
ubiquitin
E1
E2
E1
ubiquitin
ATP
ADP
Pi
Protein target
AMP
26S proteasome
19S proteasome
E1
E2
cytosol

FIGURE 2

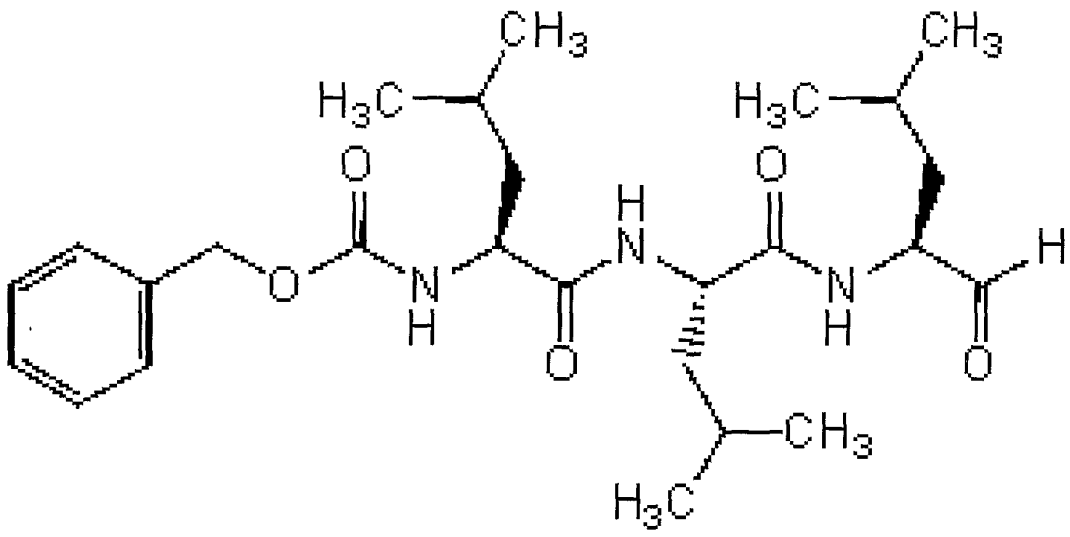


FIGURE 3A

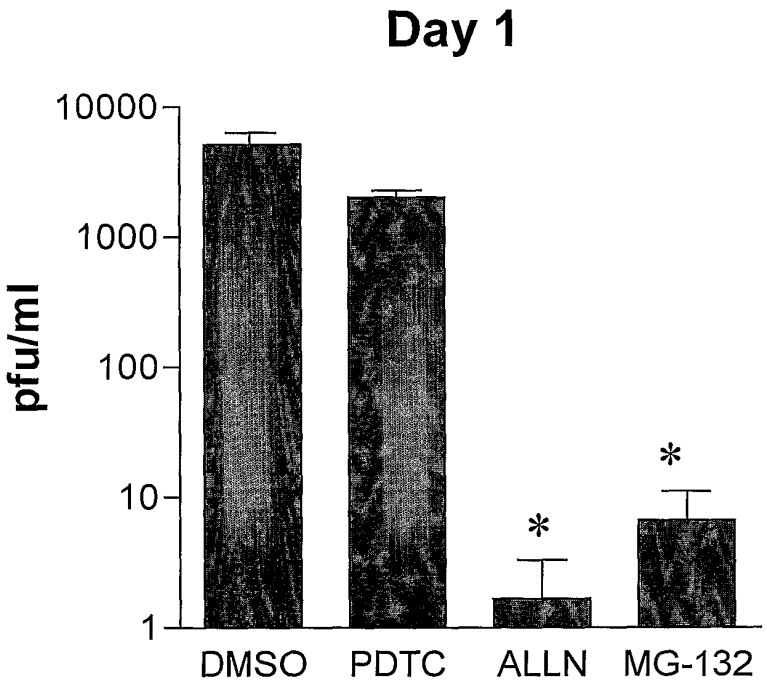


FIGURE 3B

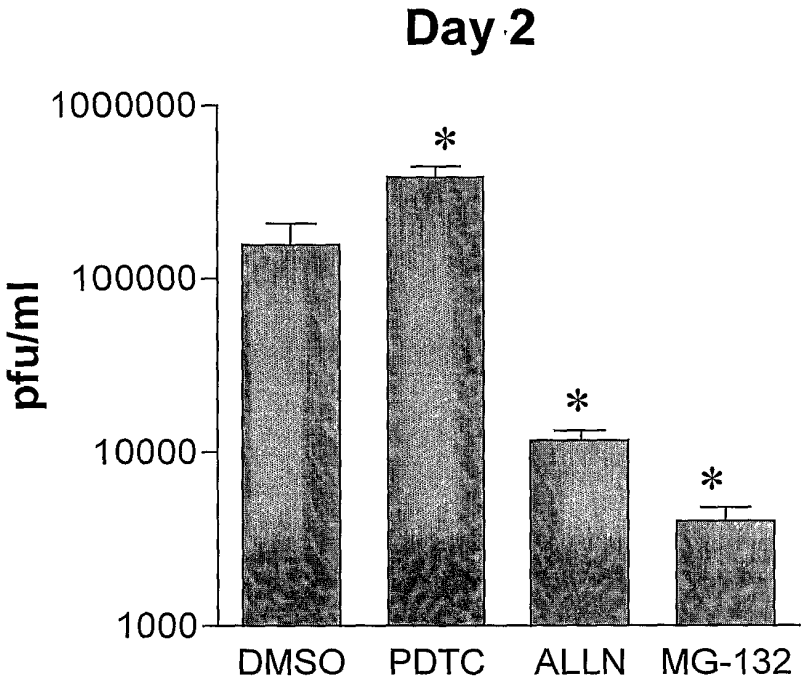


FIGURE 3C

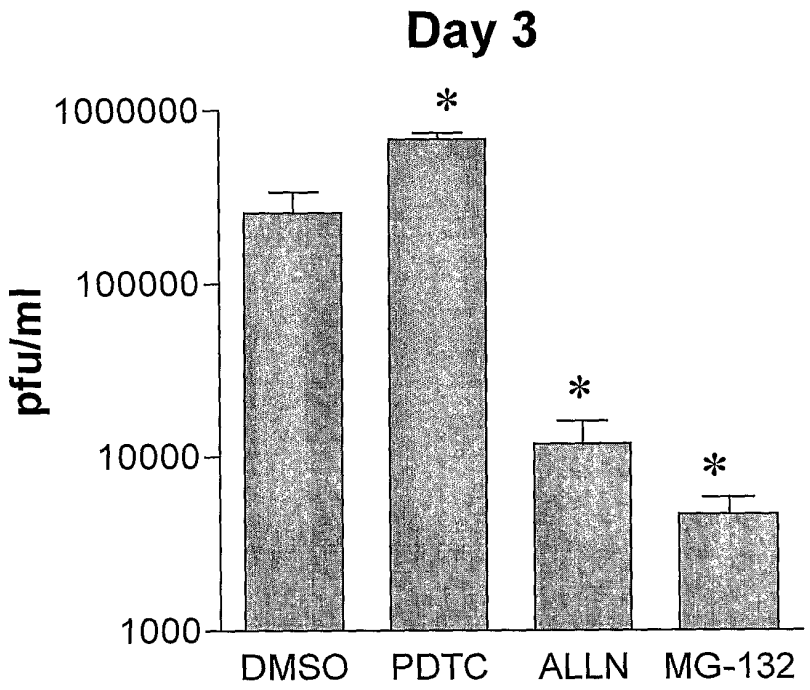


FIGURE 4A

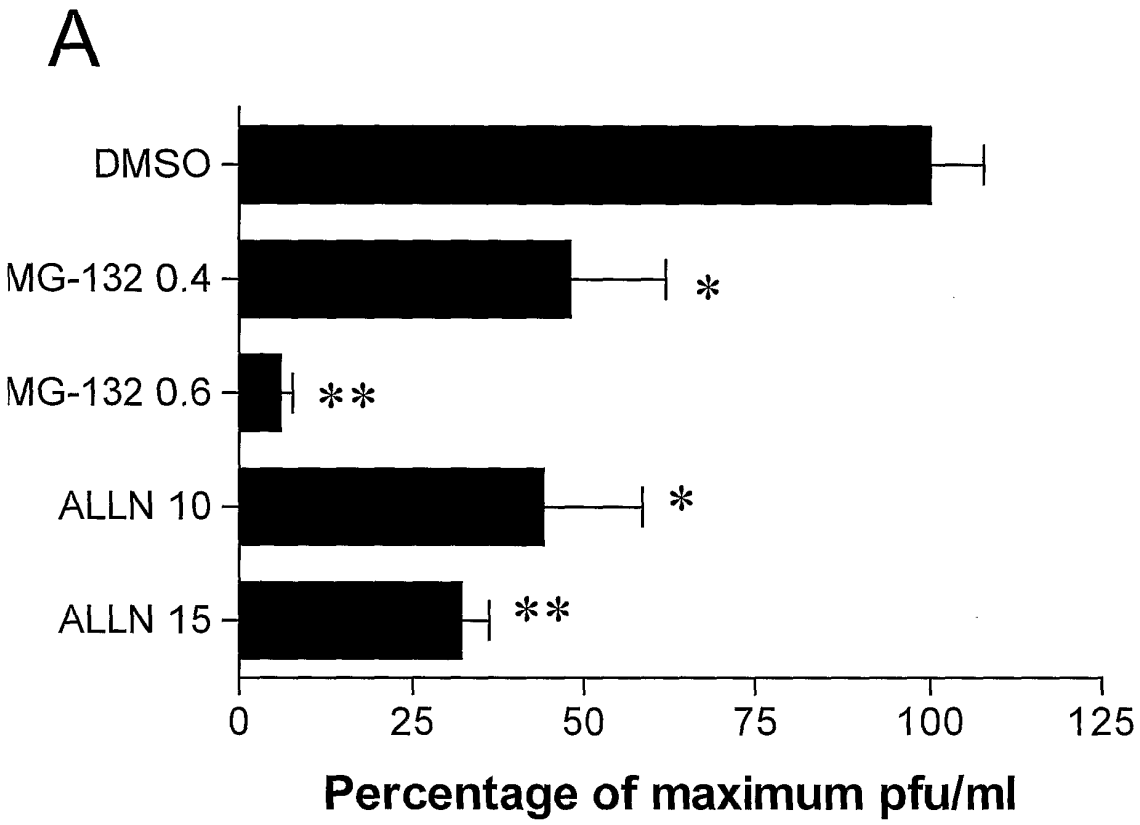

A
DMSO
MG-132 0.4
MG-132 0.6
ALLN 10
ALLN 15
*
**
*
**
0
25
50
75
100
125
Percentage of maximum pfu/ml

FIGURE 4B

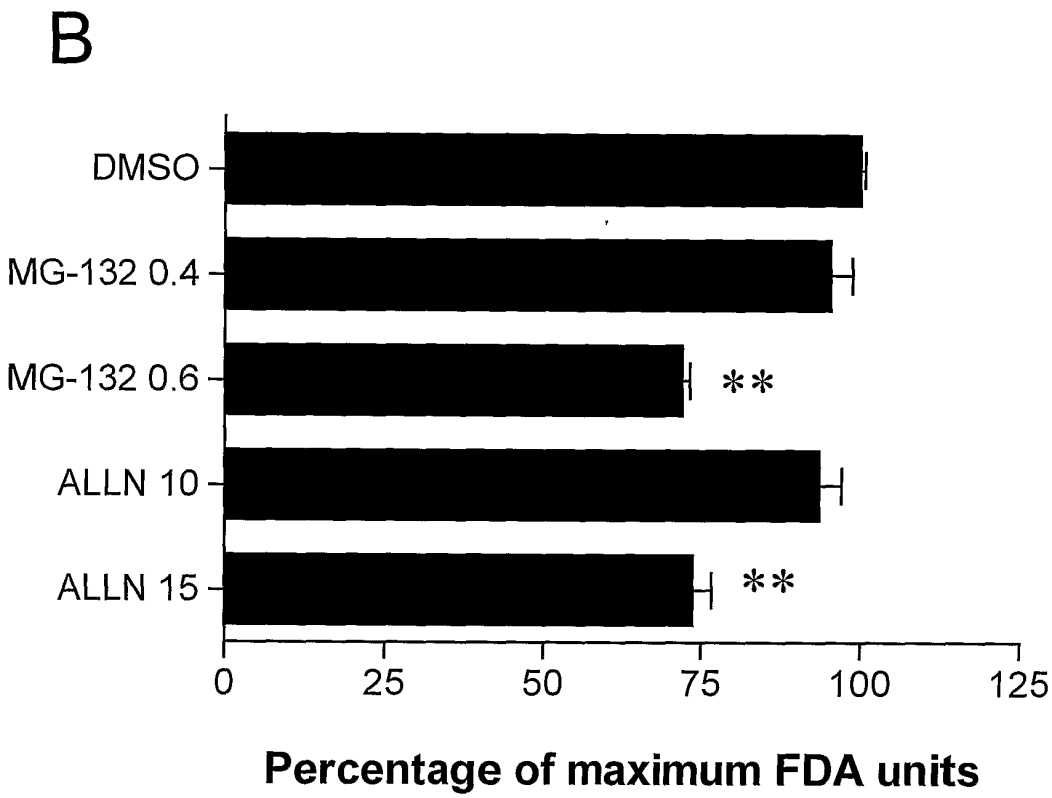

B
DMSO
MG-132 0.4
MG-132 0.6
ALLN 10
ALLN 15
**
**
0
25
50
75
100
125
Percentage of maximum FDA units

FIGURE 5A

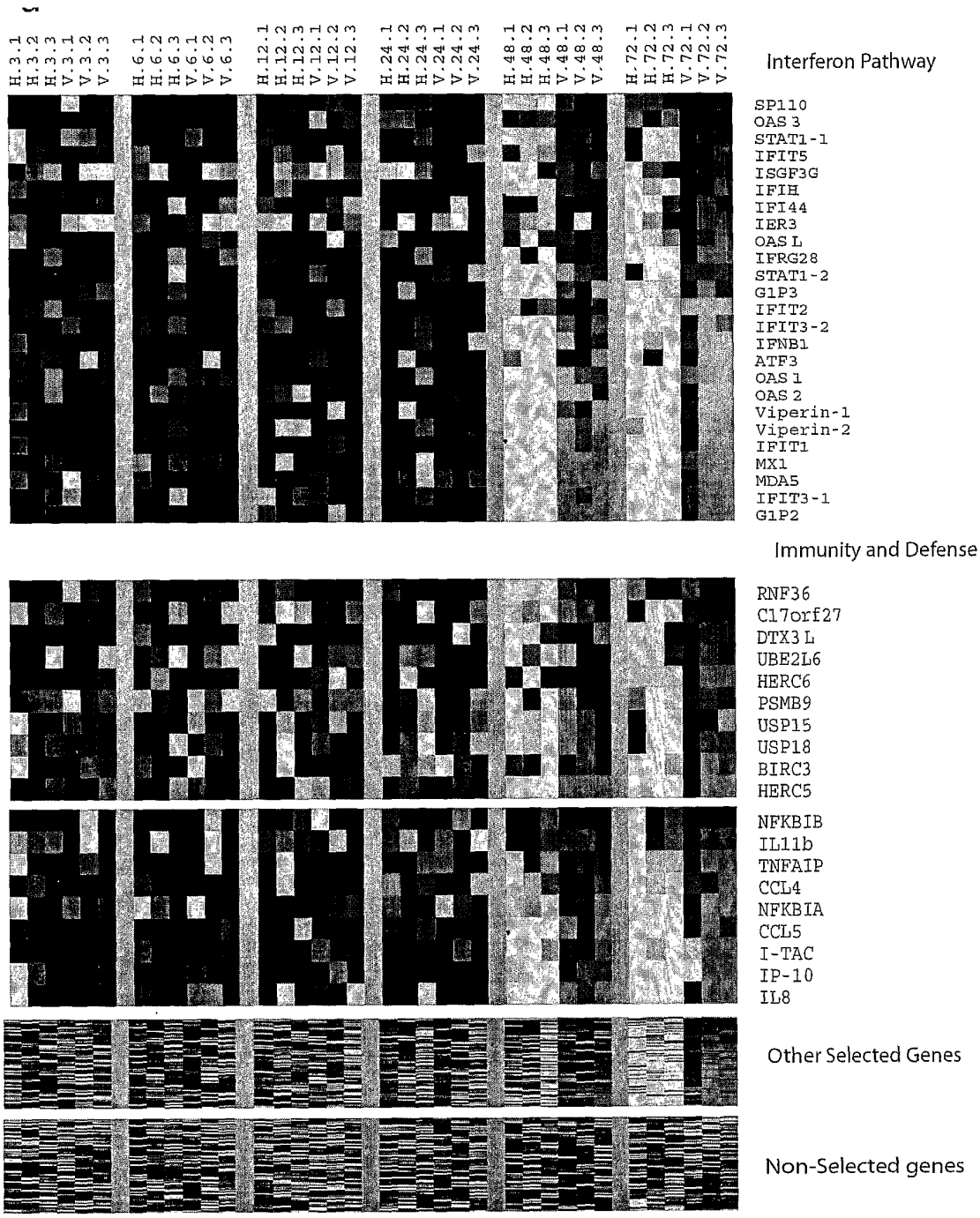

H.3.1
H.3.2
H.3.3
V.3.1
V.3.2
V.3.3
H.6.1
H.6.2
H.6.3
V.6.1
V.6.2
V.6.3
H.12.1
H.12.2
H.12.3
V.12.1
V.12.2
V.12.3
H.24.1
H.24.2
H.24.3
V.24.1
V.24.2
V.24.3
H.48.1
H.48.2
H.48.3
V.48.1
V.48.2
V.48.3
H.72.1
H.72.2
H.72.3
V.72.1
V.72.2
V.72.3
Interferon Pathway
SP110
OAS 3
STAT1-1
IFIT5
ISGF3G
IFIH
IFI44
IER3
OAS L
IFRG28
STAT1-2
G1P3
IFIT2
IFIT3-2
IFNB1
ATF3
OAS 1
OAS 2
Viperin-1
Viperin-2
IFIT1
MX1
MDA5
IFIT3-1
G1P2
Immunity and Defense
RNF36
C17orf27
DTX3 L
UBE2L6
HERC6
PSMB9
USP15
USP18
BIRC3
HERC5
NFKBIB
IL11b
TNFAIP
CCL4
NFKBIA
CCL5
I-TAC
IP-10
IL8
Other Selected Genes
Non-Selected genes

FIGURE 5B

		48 Hours			72 Hours		
Biological Process	Arrayed	SAM	Expected	P value	SAM	Expected	P value
Interferon-mediated immunity	40	9	0.13	6.64E-15	9	0.33	5.79E-11
Immunity and defense	767	13	2.45	2.66E-07	22	6.28	1.51E-07

FIGURE 6A

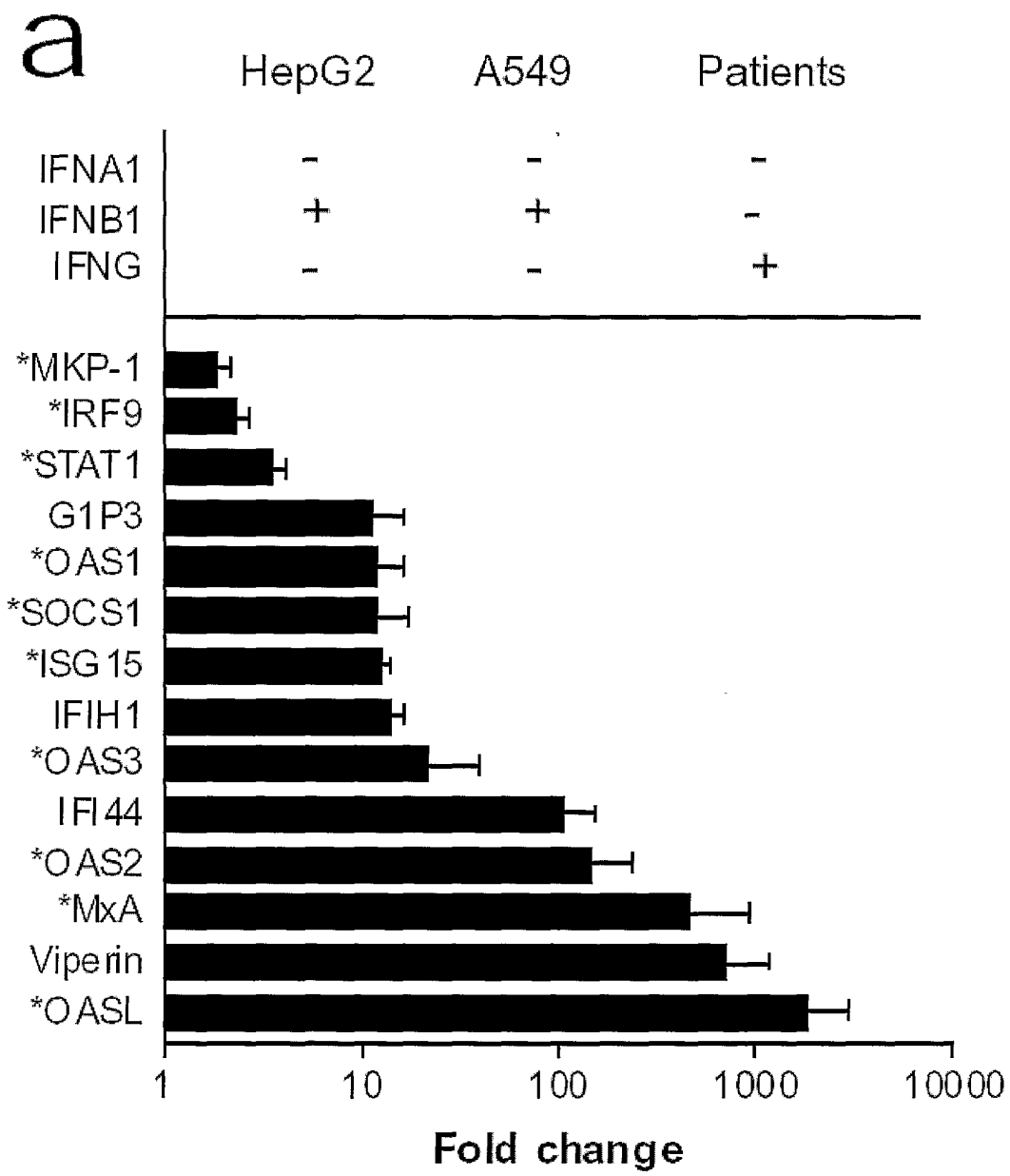

a
HepG2
A549
Patients
IFNA1
IFNB1
IFNG
- - -
+ + -
- - +
*MKP-1
*IRF9
*STAT1
G1P3
*OAS1
*SOCS1
*ISG15
IFIH1
*OAS3
IFI44
*OAS2
*MxA
Viperin
*OASL
1
10
100
1000
10000
Fold change

FIGURE 6B

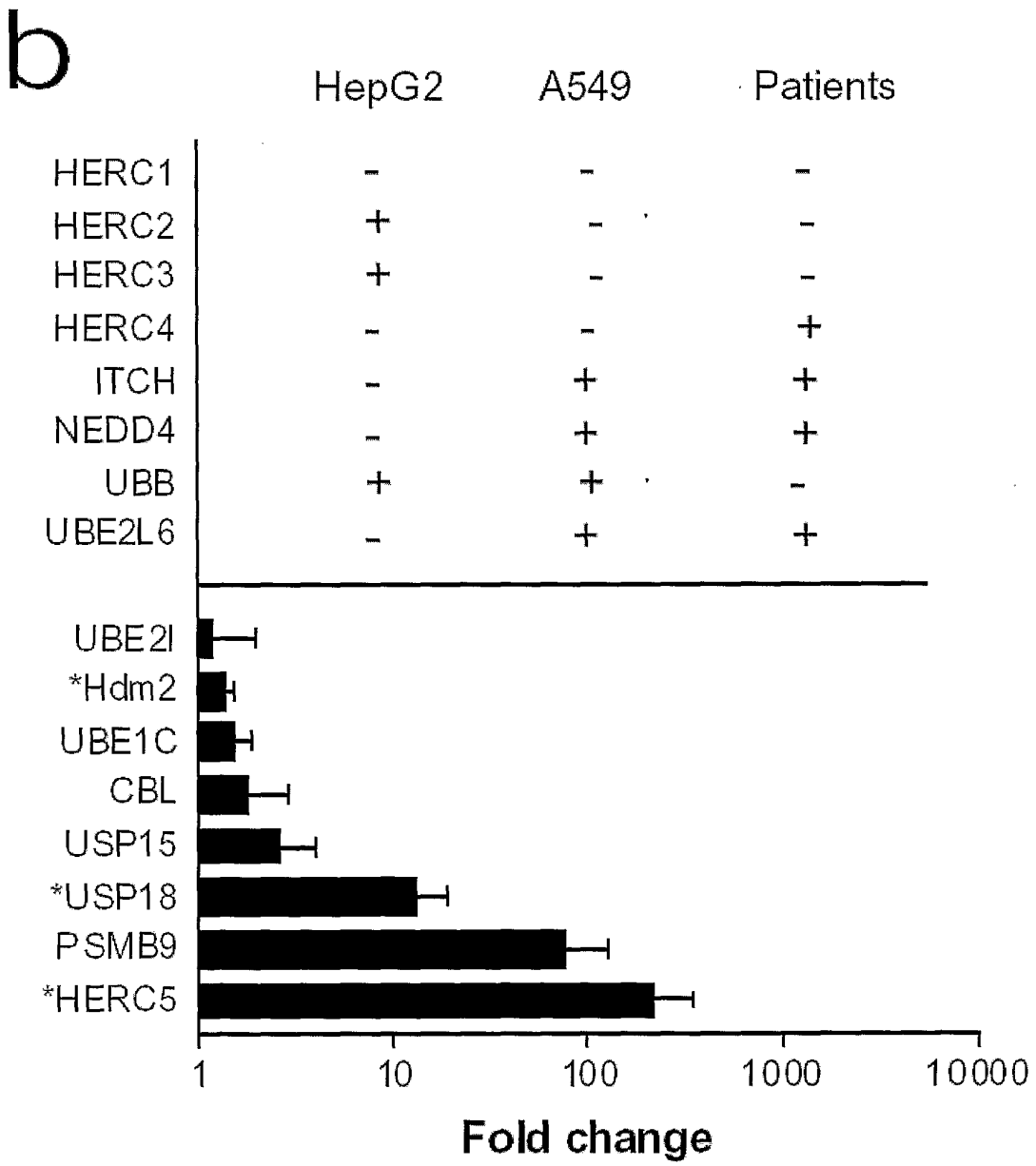

b
HepG2
A549
Patients
HERC1 - - -
HERC2 + - -
HERC3 + - -
HERC4 - - +
ITCH - + +
NEDD4 - + +
UBB + + -
UBE2L6 - + +
UBE2I
*Hdm2
UBE1C
CBL
USP15
*USP18
PSMB9
*HERC5
1
10
100
1000
10000
Fold change

FIGURE 6C

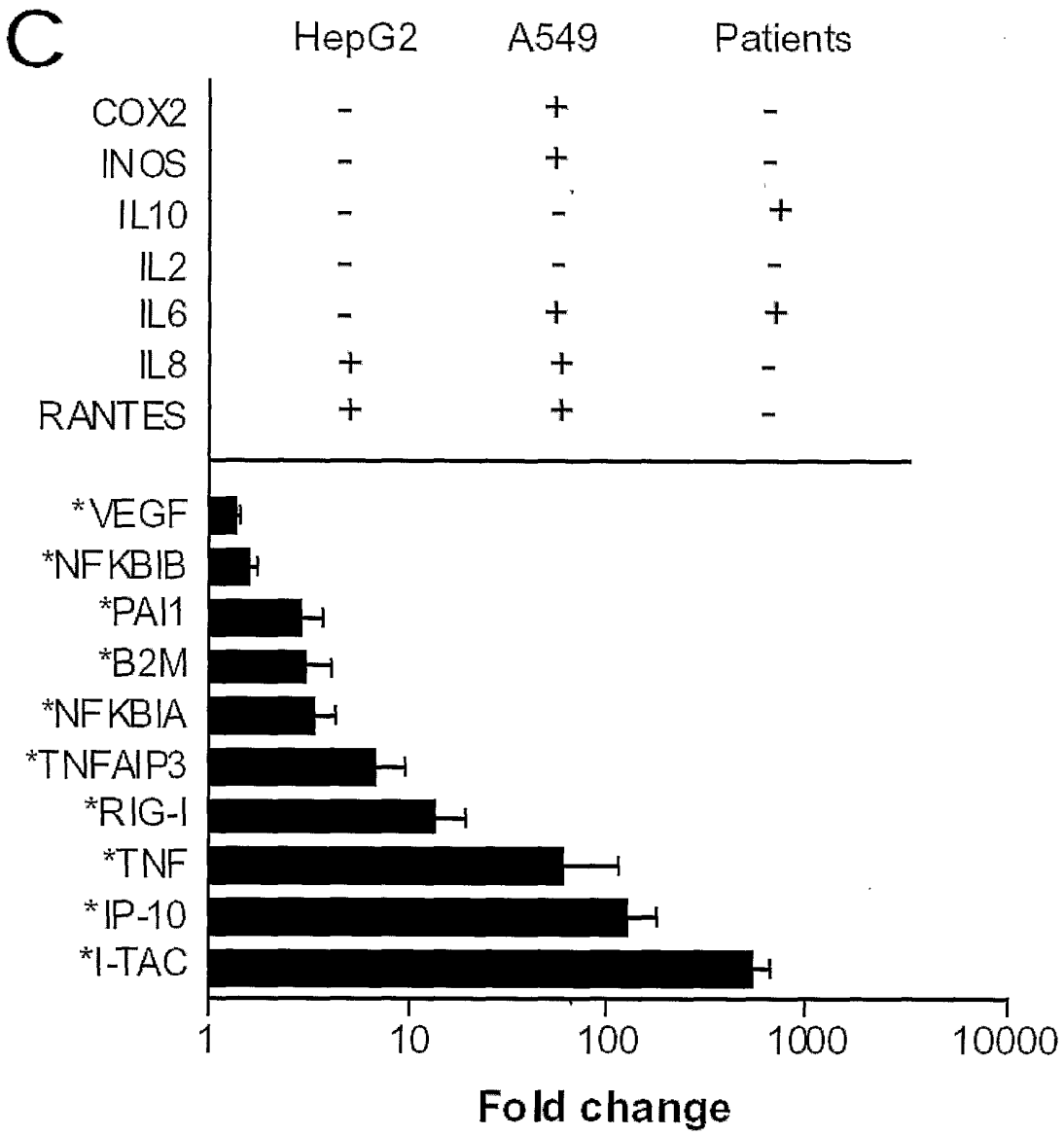
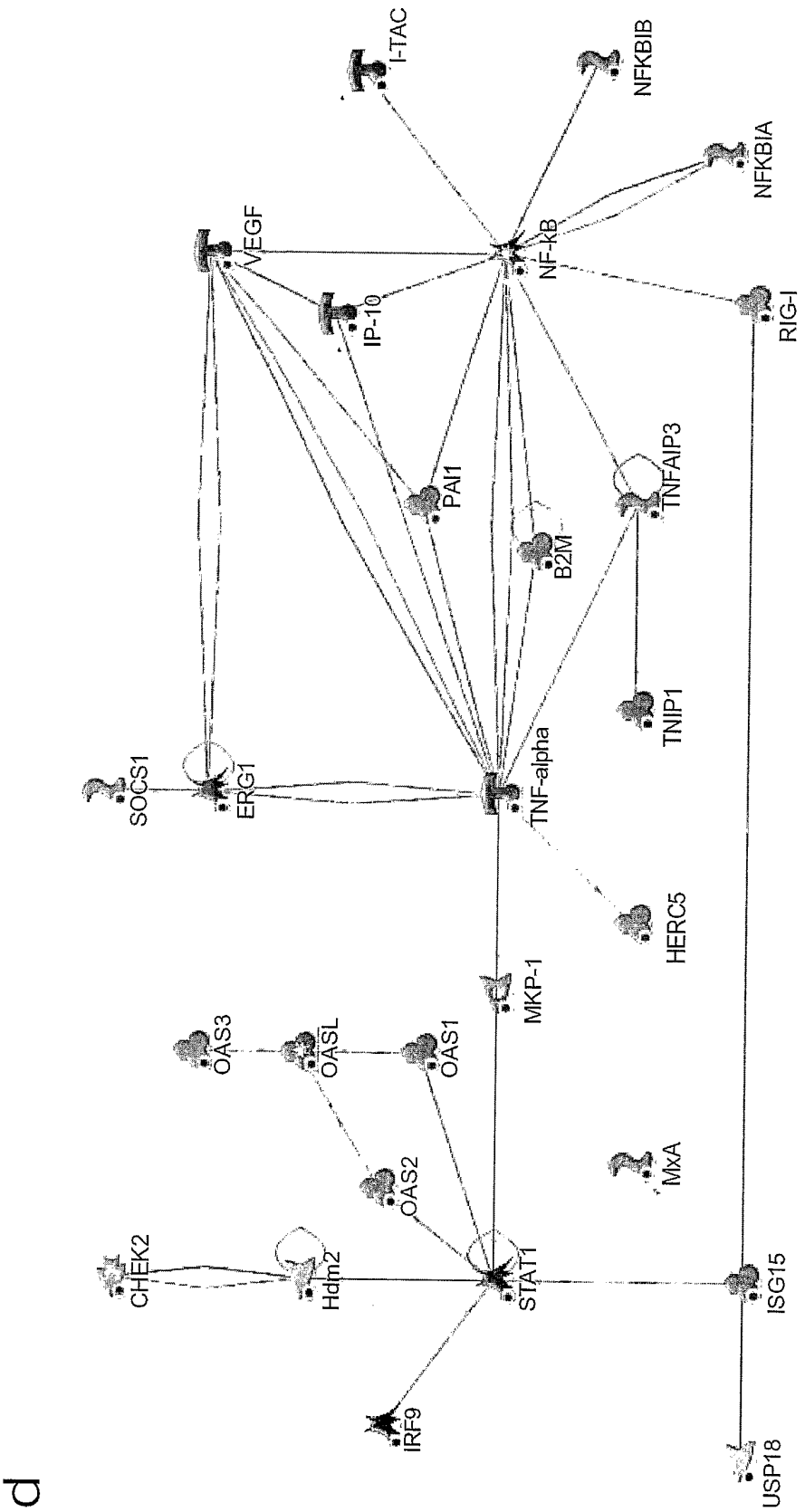

C
HepG2
A549
Patients
COX2 - + -
INOS - + -
IL10 - - +
IL2 - - -
IL6 - + +
IL8 + + -
RANTES + + -
*VEGF
*NFKBIB
*PAI1
*B2M
*NFKBIA
*TNFAIP3
*RIG-I
*TNF
*IP-10
*I-TAC
1
10
100
1000
10000
Fold change

FIGURE 6D


I-TAC
NFKBIB
NFKBIA
VEGF
NF-kB
IP-10
RIG-I
PAI1
TNFAIP3
B2M
TNIP1
SOCS1
ERG1
TNF-alpha
HERC5
MKP-1
OAS3
OASL
OAS1
MxA
OAS2
CHEK2
Hdm2
STAT1
ISG15
IRF9
USP18

d

FIGURE 7A

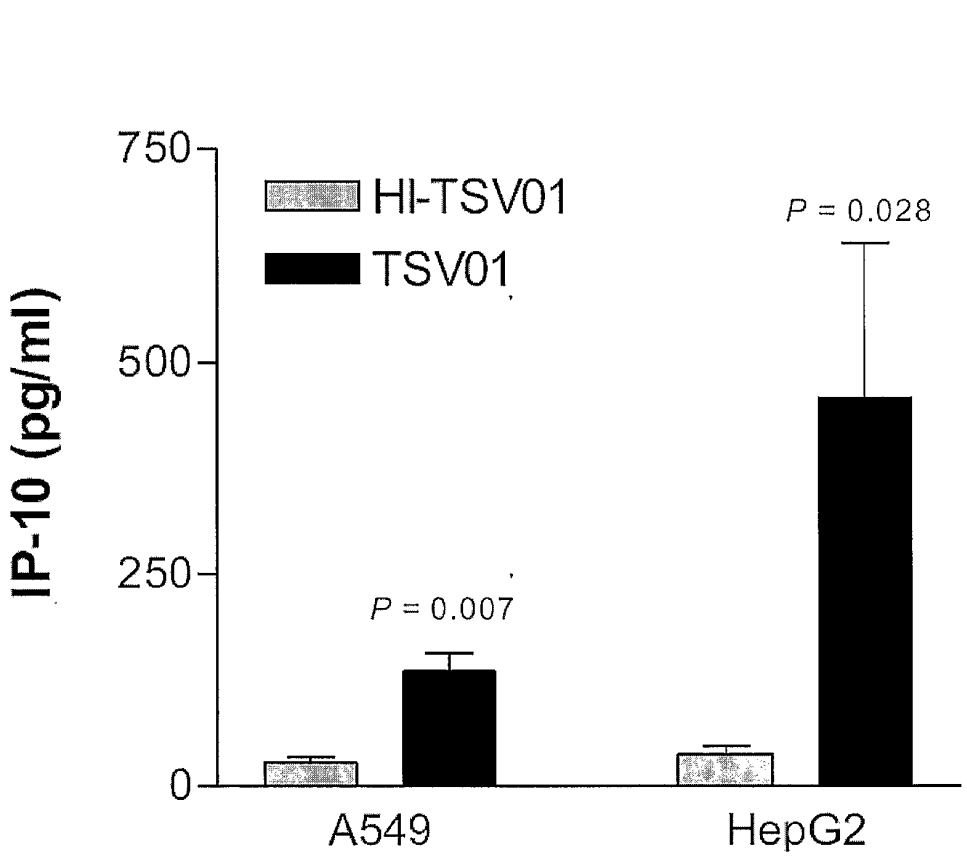

a
750
500
250
0
IP-10 (pg/ml)
HI-TSV01
TSV01
P = 0.007
P = 0.028
A549
HepG2

FIGURE 7B

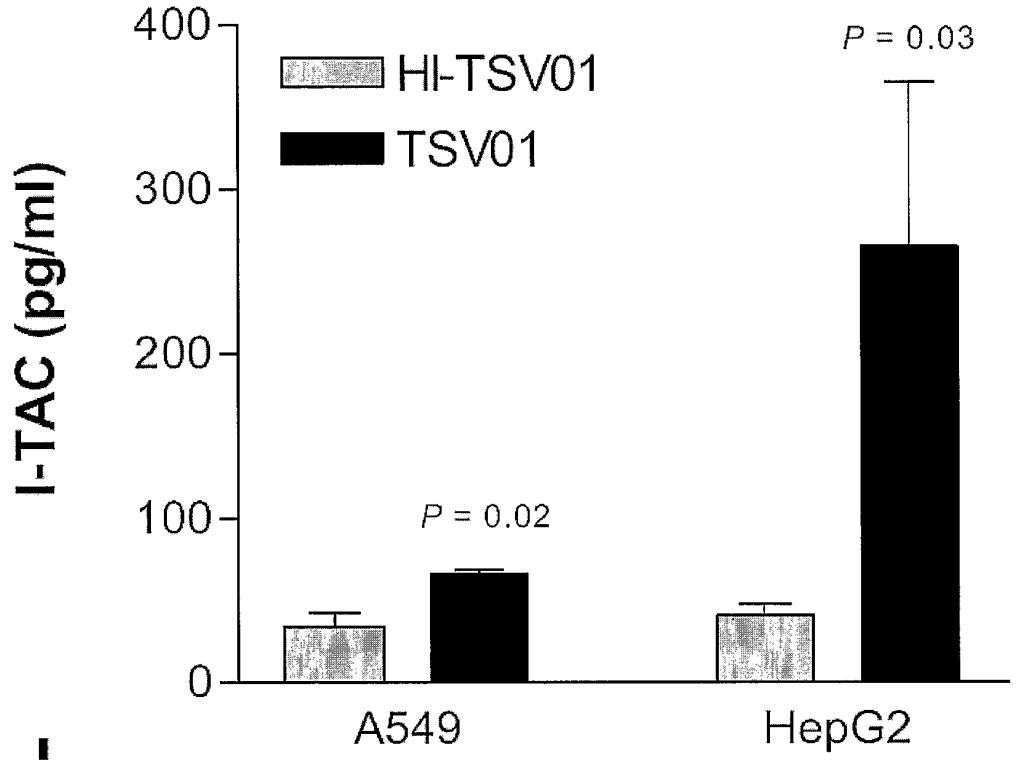

400
300
200
100
0
I-TAC (pg/ml)
HI-TSV01
TSV01
P = 0.02
P = 0.03
A549
HepG2

FIGURE 7C

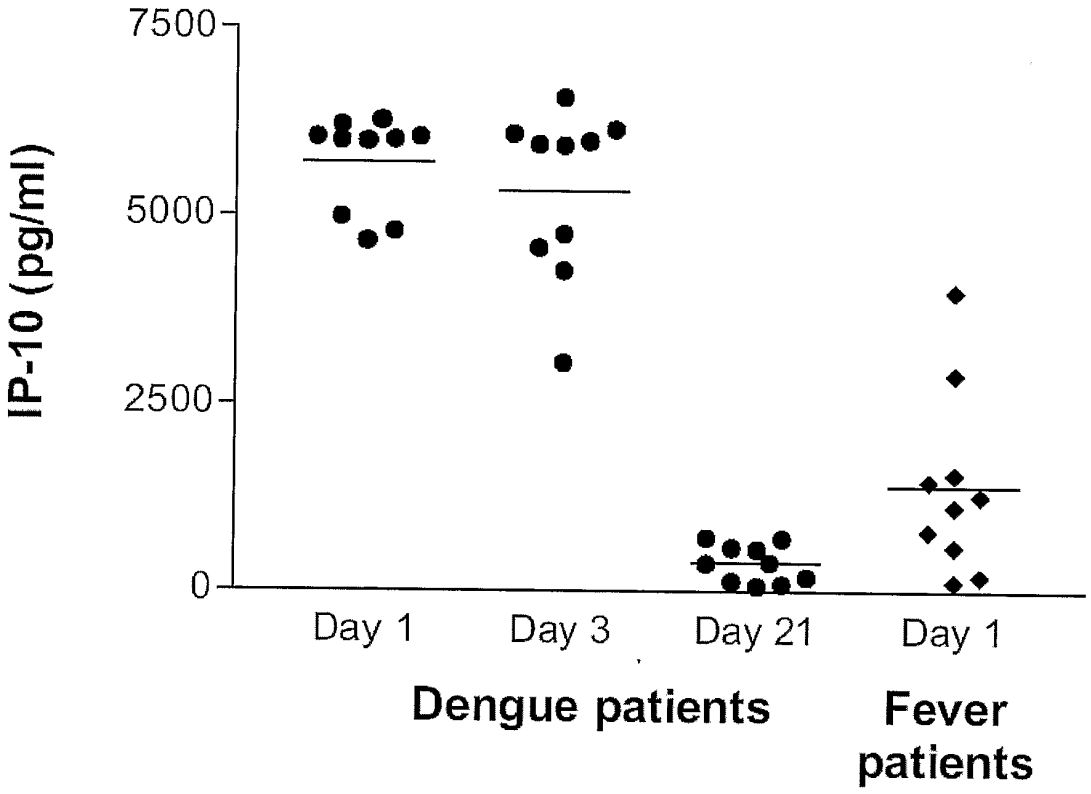

IP-10 (pg/ml)
7500
5000
2500
0
Day 1
Day 3
Day 21
Day 1
Dengue patients
Fever patients

FIGURE 7D

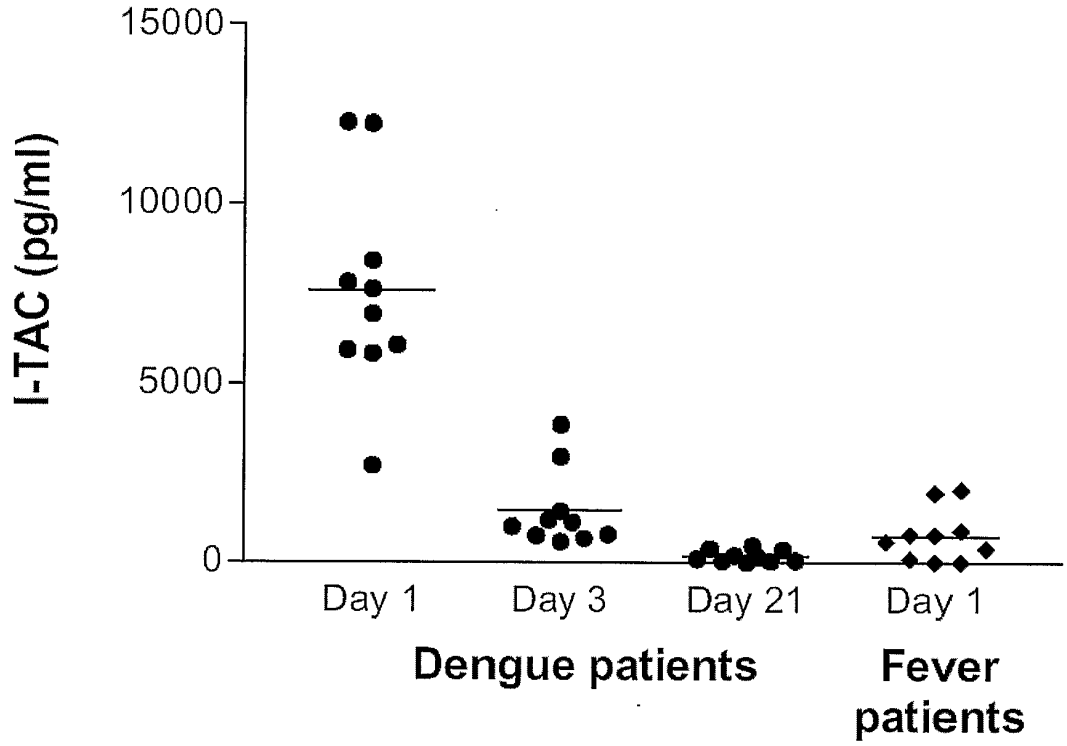

15000
10000
5000
0
I-TAC (pg/ml)
Day 1
Day 3
Day 21
Day 1
Dengue patients
Fever patients

FIGURE 7E

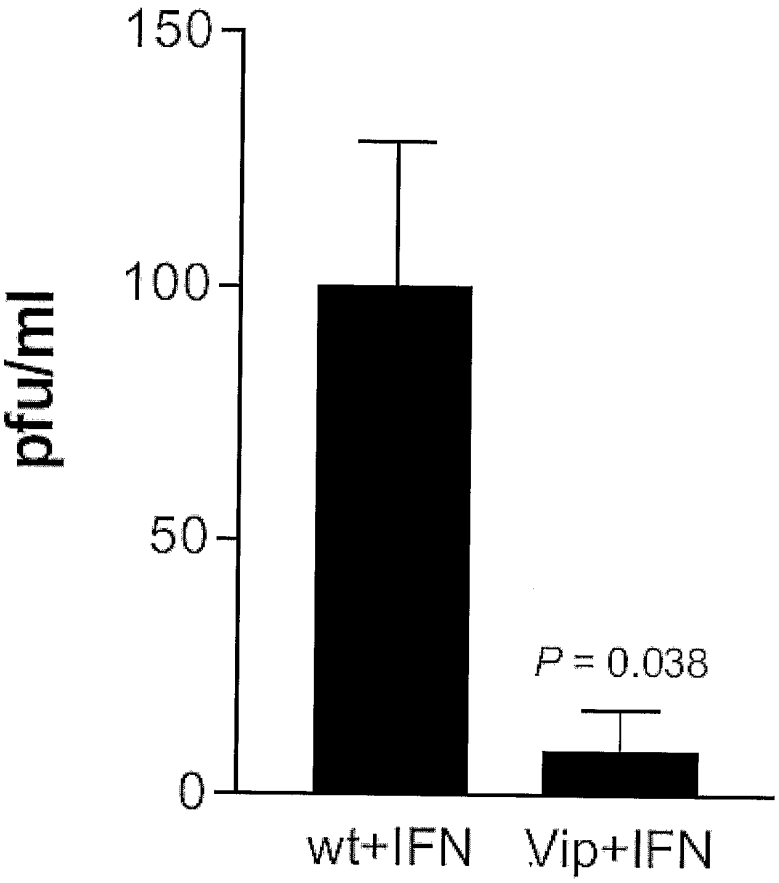


FIGURE 7F

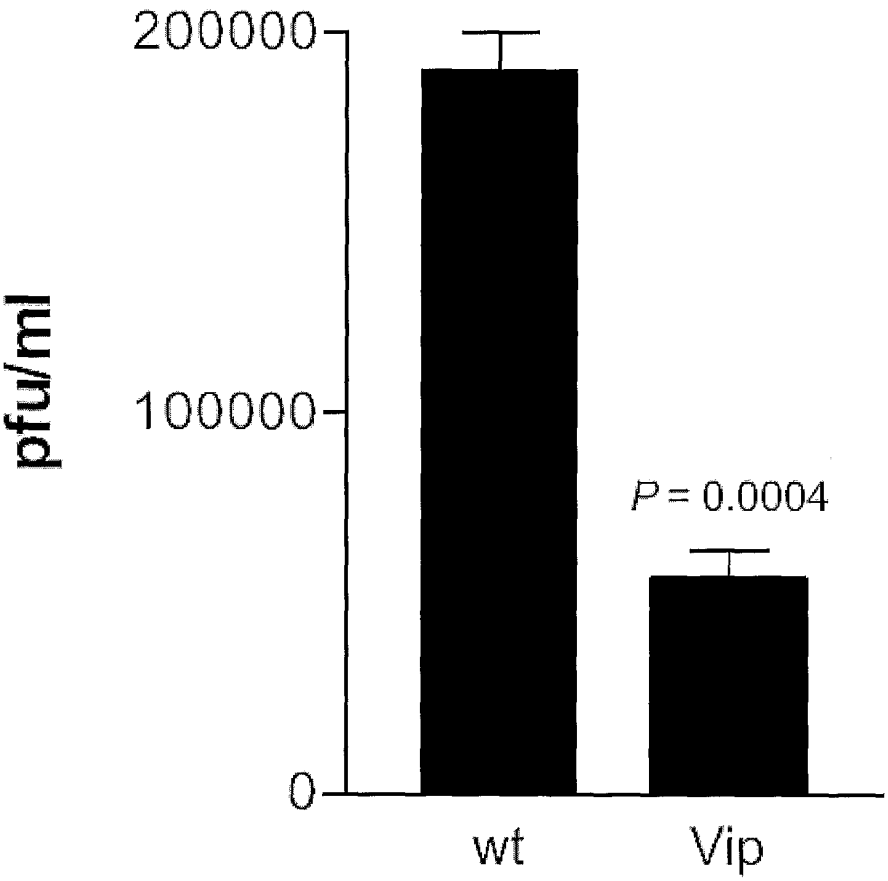


FIGURE 7G

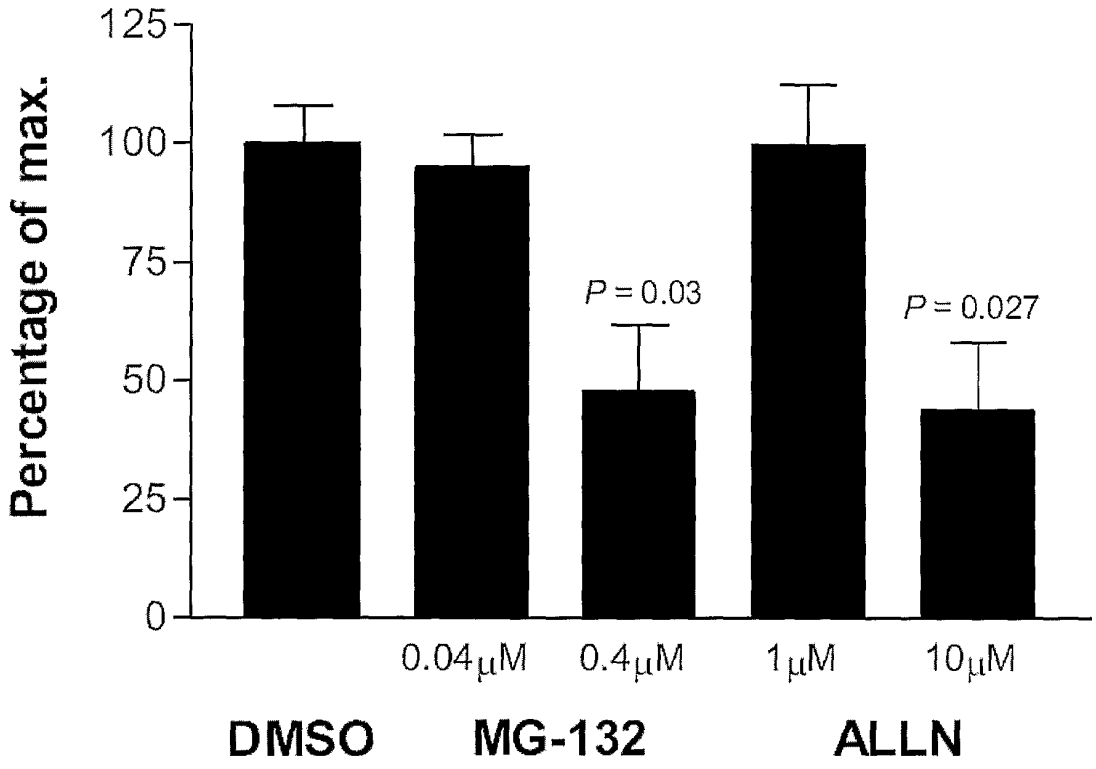

Percentage of max.
125
100
75
50
25
0
P = 0.03
P = 0.027
0.04μM
0.4μM
1μM
10μM
DMSO
MG-132
ALLN

FIGURE 8A

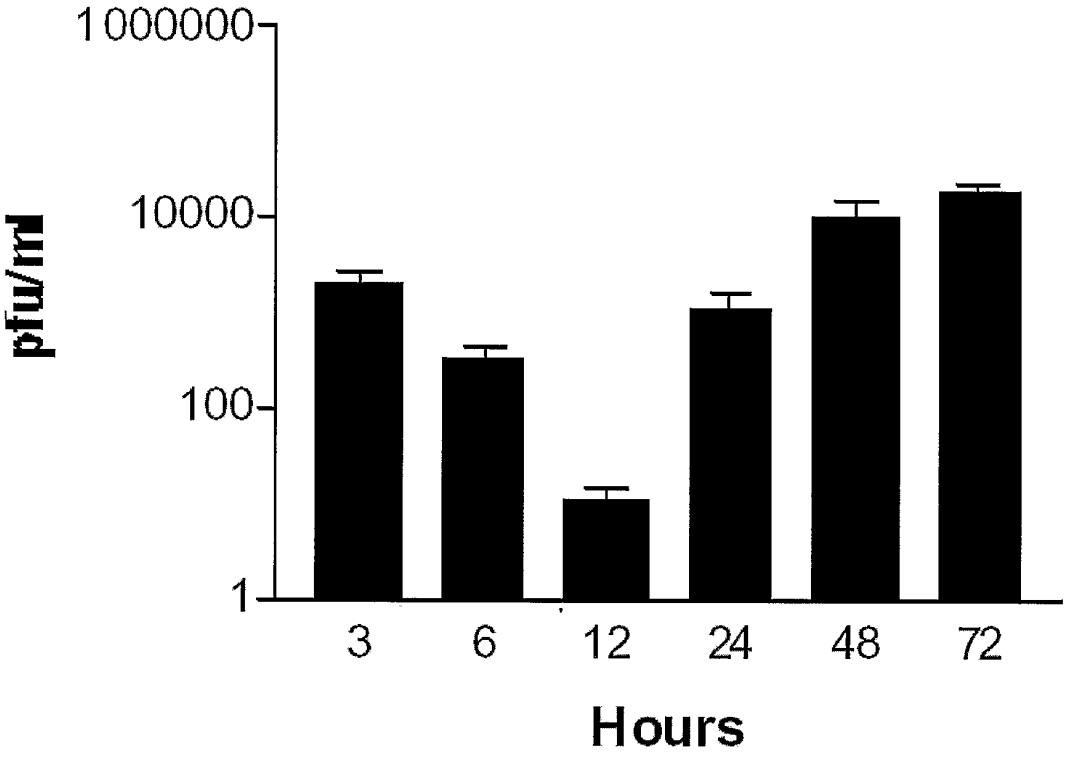


FIGURE 8B

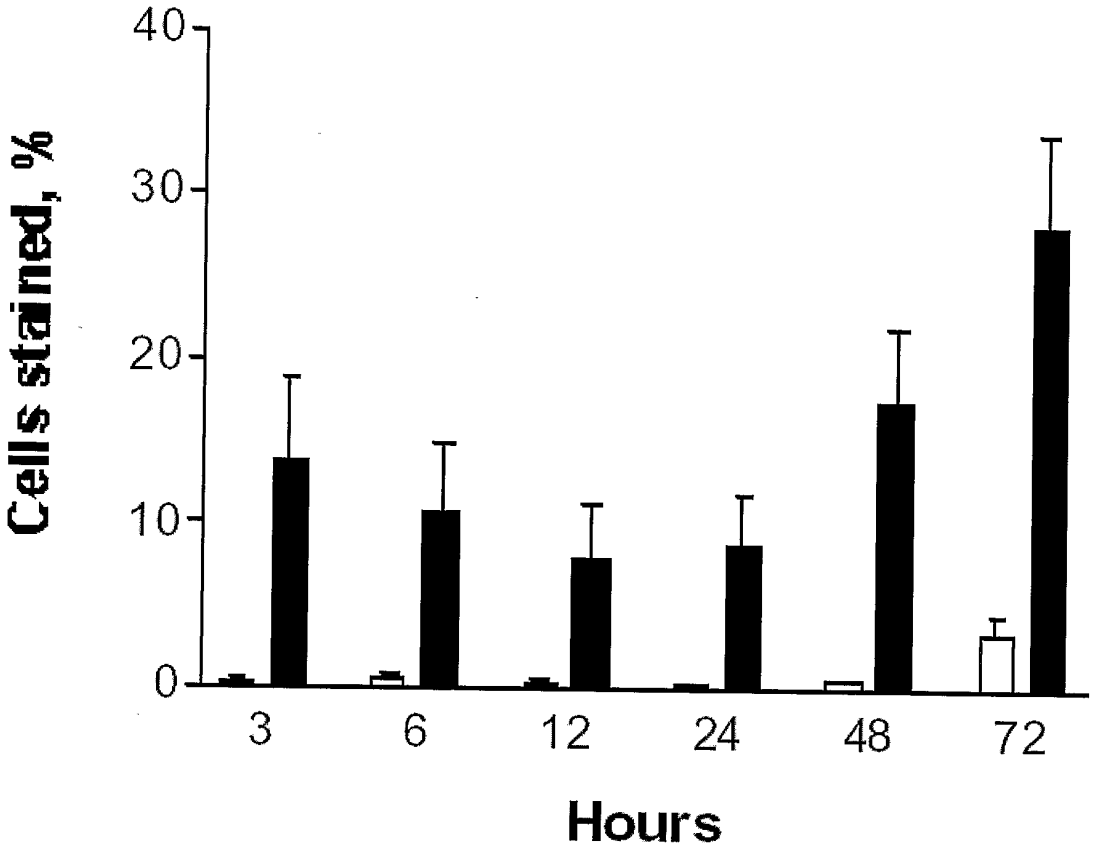
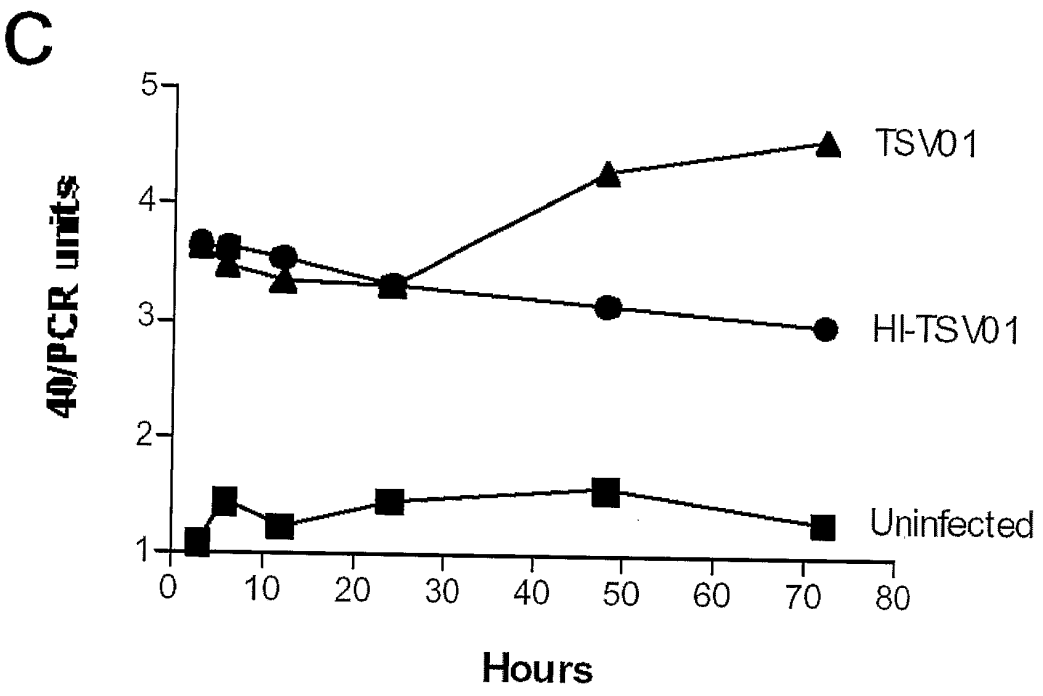


FIGURE 8C


C
40/PCR units
5
4
3
2
1
0
10
20
30
40
50
60
70
80
Hours
TSV01
HI-TSV01
Uninfected