

FIGURE 1

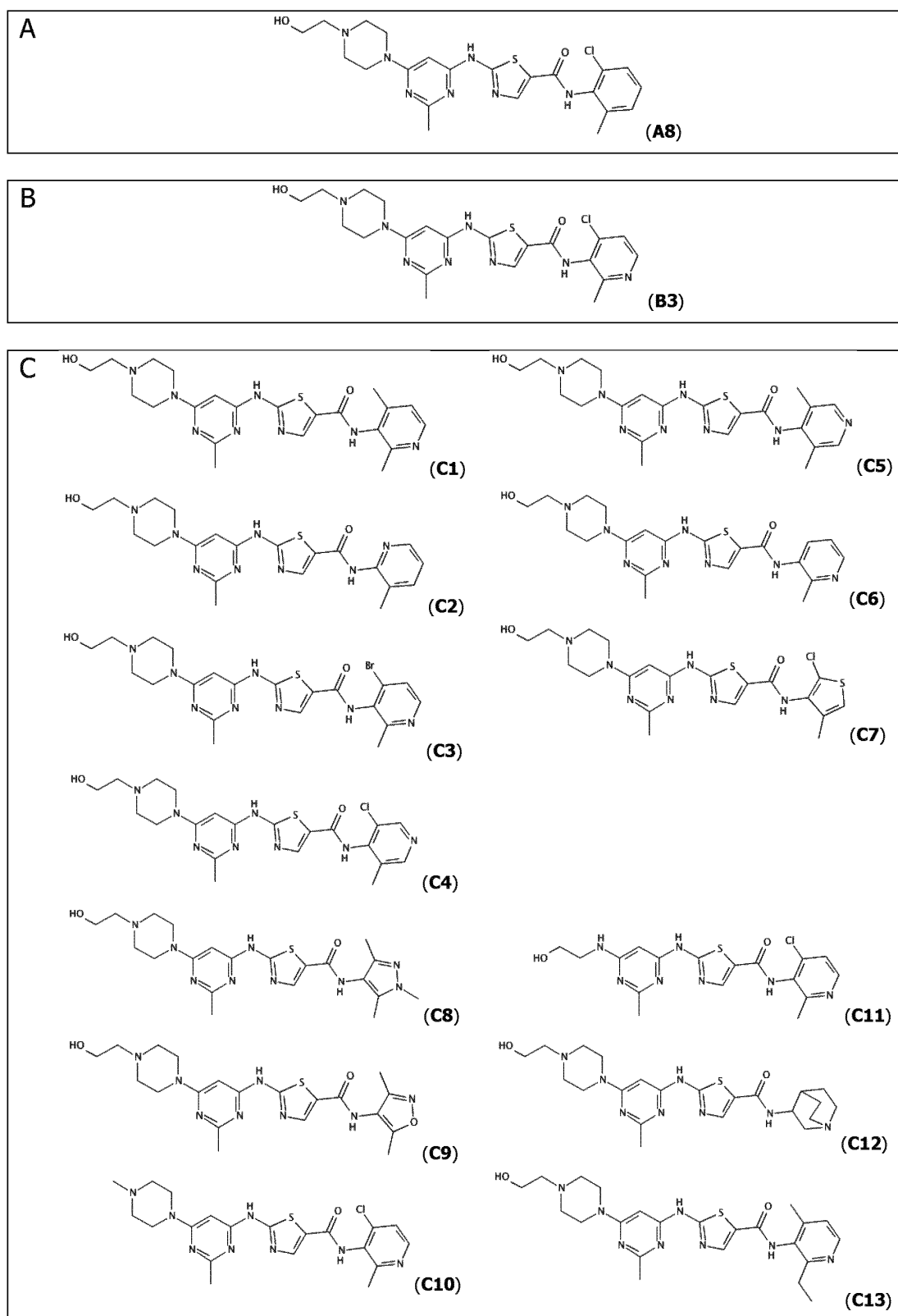


FIGURE 1 (CONT)

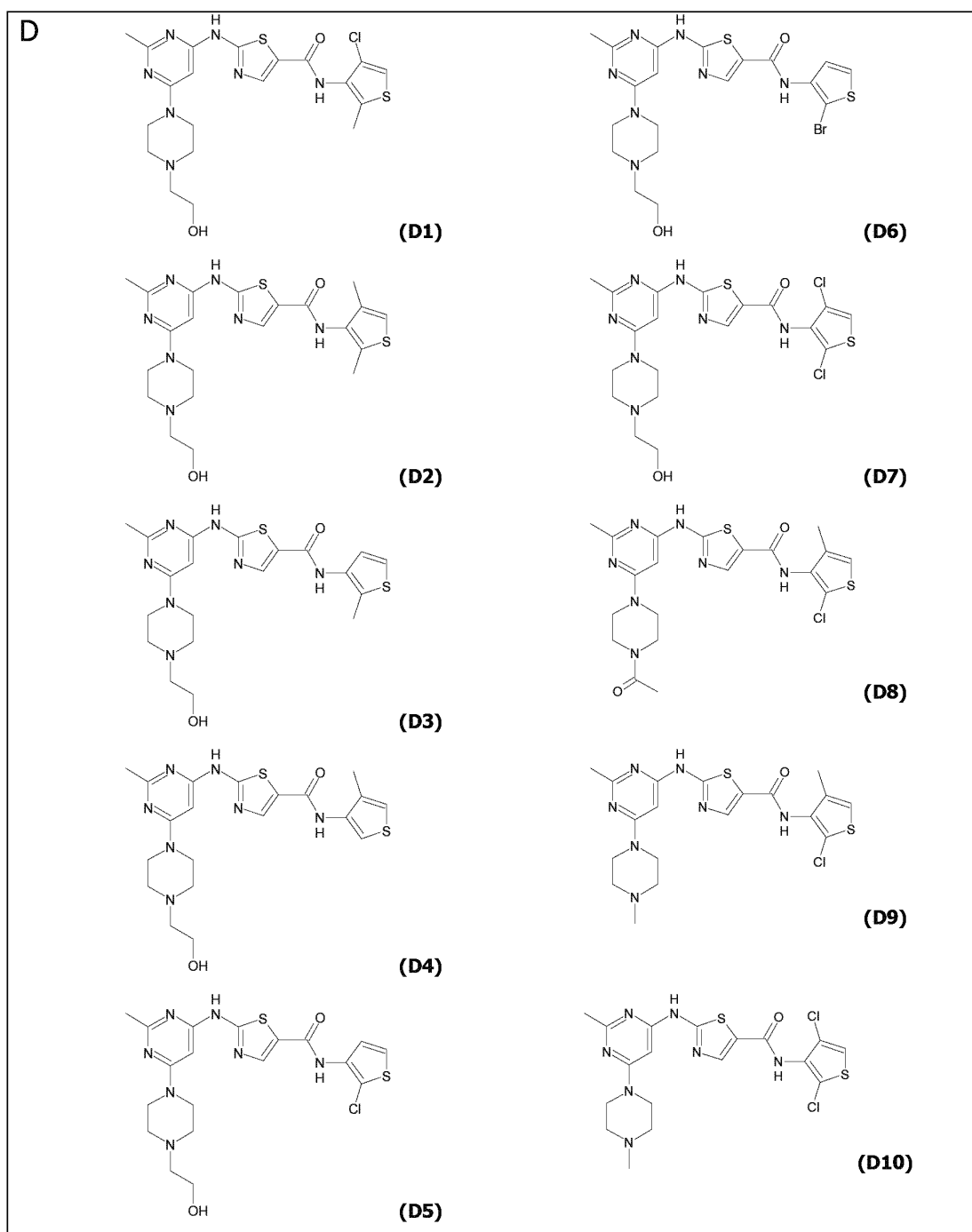


FIGURE 1 (CONT)

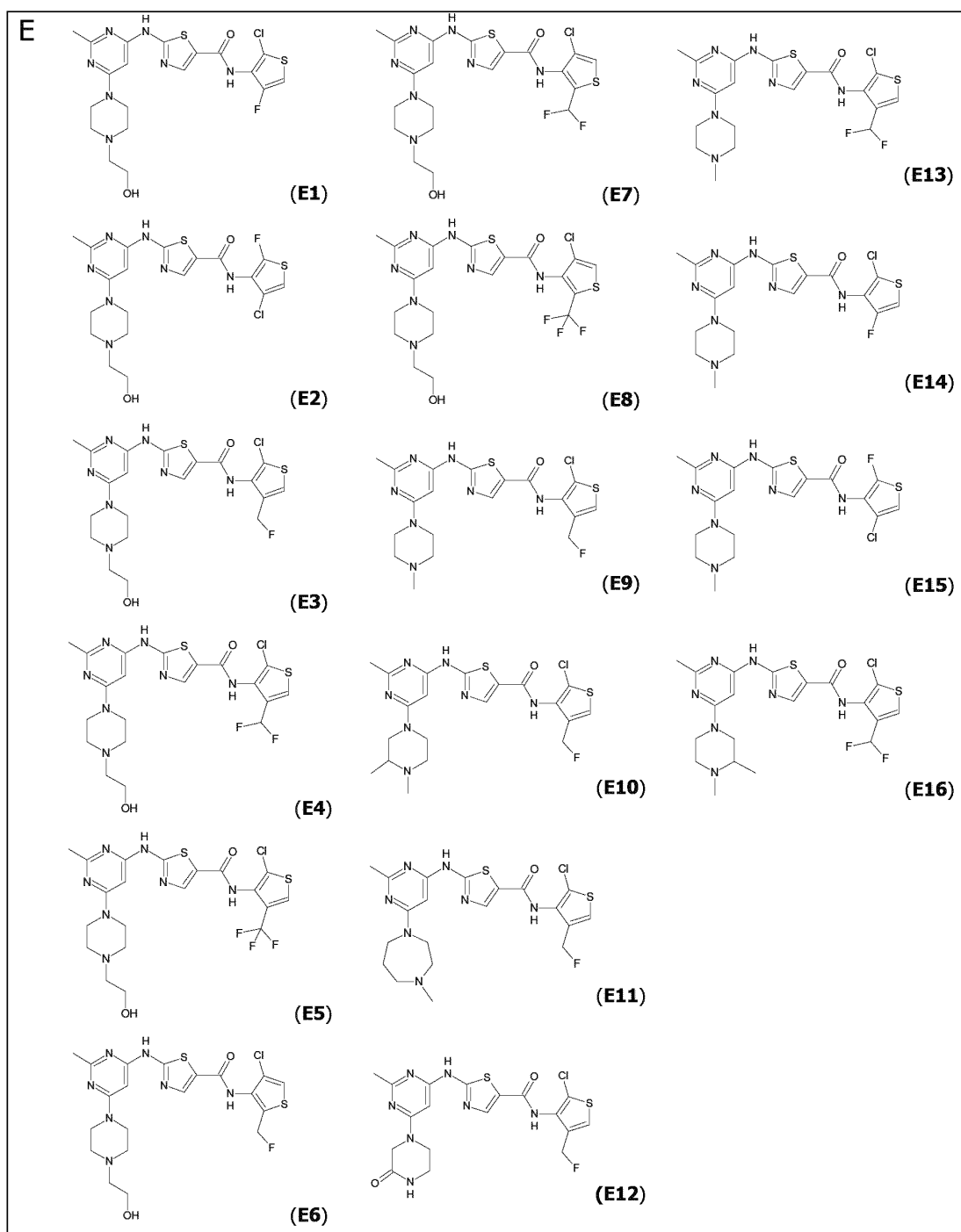


FIGURE 2

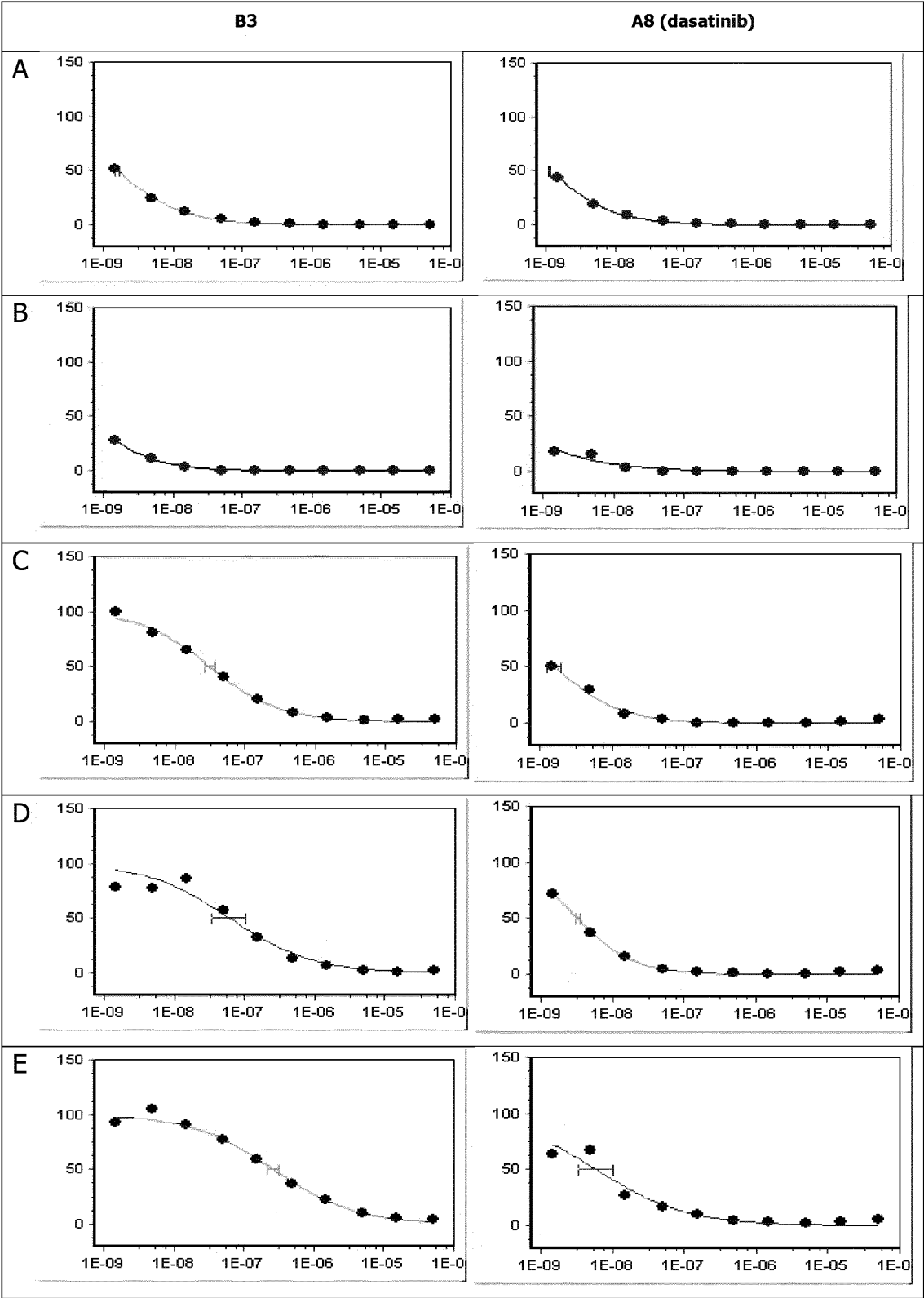


FIGURE 2 (Cont)

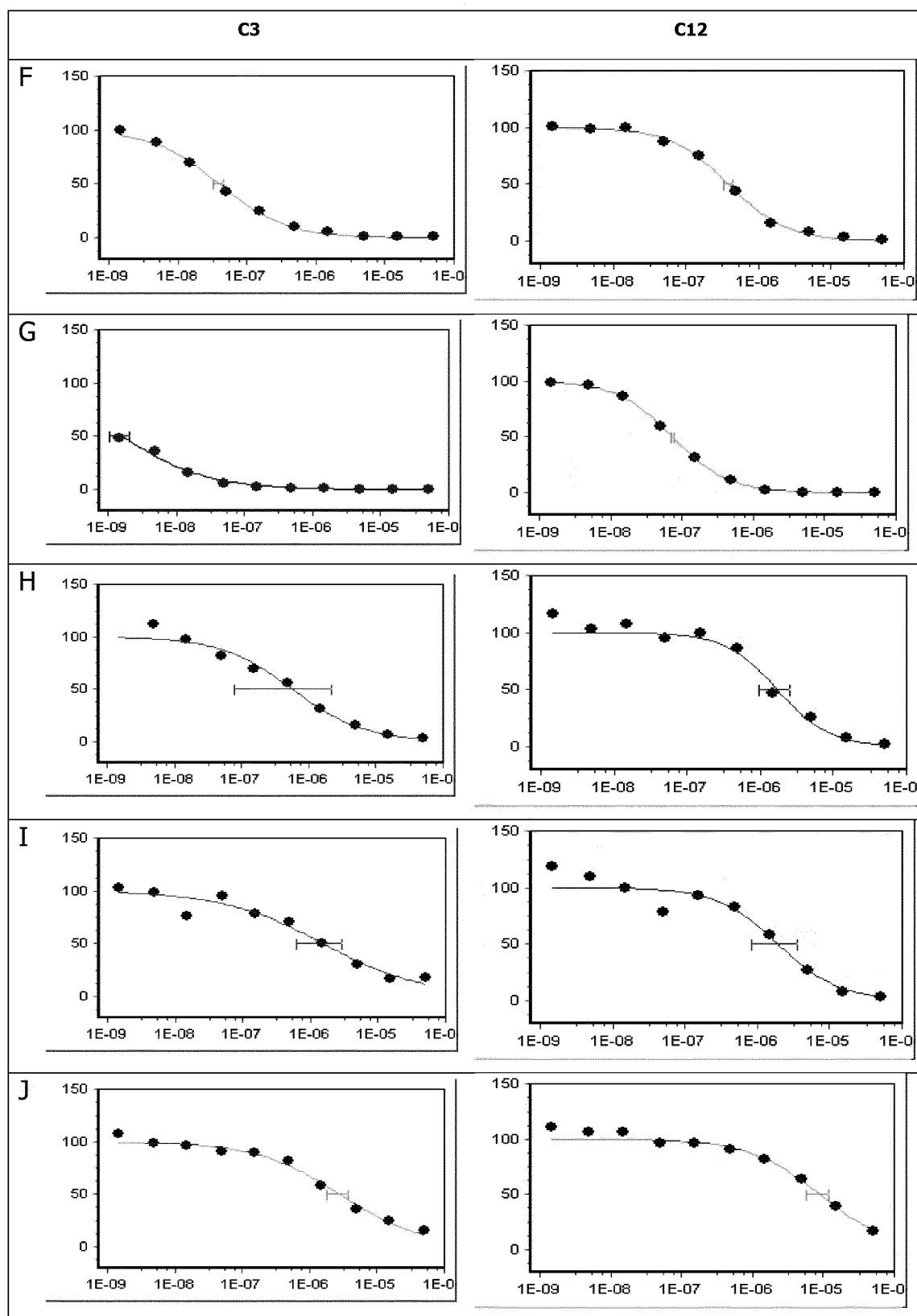


FIGURE 3

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
ABL1	TK	****	****	****
ABL2	TK	****	****	****
ACK1	TK	****	****	****
ACV-R1	TKL	***	****	****
ACV-R1B	TKL	***	****	****
ACV-R2A	TKL	***	****	****
ACV-R2B	TKL	**	****	****
ACV-RL1	TKL	***	****	****
AKT1 aa106-480	AGC	*	*	*
AKT2 aa107-481	AGC	*	*	*
AKT3 aa106-479	AGC	*	*	*
ALK (GST-HIS-tag)	TK	*	*	*
AMPK-alpha1 aa1-550	CAMK	*	*	*
ARK5	CAMK	*	*	*
ASK1	STE	*	*	*
Aurora-A	OTHER	*	**	***
Aurora-B	OTHER	*	*	***
Aurora-C	OTHER	*	*	*
AXL	TK	**	*	*
BLK	TK	****	****	****
BMPR1A	TKL	*	***	***
BMX	TK	****	****	****
B-RAF	TKL	***	****	****
BRK	TK	****	****	****
BRSK1	CAMK	*	*	*
BRSK2	CAMK	*	*	*
BTK	TK	****	****	****
BUB1B	OTHER	*	*	*
CAMK1D	CAMK	*	*	*
CAMK2A	CAMK	*	*	*
CAMK2B	CAMK	*	*	*
CAMK2D	CAMK	*	*	*
CAMK2G	CAMK	*	*	*
CAMK4	CAMK	*	*	*
CAMKK1	OTHER	*	*	*
CAMKK2	OTHER	*	*	*
CDC42BPA	AGC	*	*	**
CDC42BPB	AGC	*	*	*
CDC7/DBF4	OTHER	*	*	*
CDK1/CycA2	CMGC	*	*	*
CDK1/CycB1	CMGC	*	*	*
CDK1/CycE1	CMGC	*	*	*

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
CDK16/CycY	CMGC	*	*	*
CDK19/CycC	CMGC	*	*	*
CDK2/CycA2	CMGC	*	*	*
CDK2/CycE1	CMGC	*	*	*
CDK3/CycC	CMGC	*	*	*
CDK3/CycE1	CMGC	*	*	*
CDK4/CycD1	CMGC	*	*	*
CDK4/CycD3	CMGC	*	*	*
CDK5/p25NCK	CMGC	*	*	*
CDK5/p35NCK	CMGC	*	*	*
CDK6/CycD1	CMGC	*	*	*
CDK6/CycD3	CMGC	*	*	*
CDK7/CycH/MAT1	CMGC	*	*	*
CDK8/CycC	CMGC	*	*	*
CDK9/CycK	CMGC	*	*	*
CDK9/CycT1	CMGC	*	*	*
CHK1	CAMK	*	*	*
CHK2	CAMK	*	*	*
CK1-alpha1	CK1	*	*	*
CK1-delta	CK1	*	*	*
CK1-epsilon	CK1	*	*	*
CK1-gamma1	CK1	*	*	*
CK1-gamma2	CK1	*	*	*
CK1-gamma3	CK1	*	*	*
CK2-alpha1	OTHER	*	*	*
CK2-alpha2	OTHER	*	*	*
CLK1	CMGC	*	*	*
CLK2	CMGC	*	*	*
CLK3	CMGC	*	*	*
CLK4	CMGC	*	*	*
COT	STE	*	*	*
CSF1R	TK	****	****	****
CSK	TK	****	****	****
DAPK1	CAMK	*	*	*
DAPK2	CAMK	*	*	*
DAPK3	CAMK	*	*	*
DCAMKL2	CAMK	*	*	*
DDR2	TK	****	****	****
DMPK	AGC	*	*	**
DNA-PK	ATYPICAL	*	*	*
DYRK1A	CMGC	*	*	*
DYRK1B	CMGC	*	*	*

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
DYRK2	CMGC	*	*	*
DYRK3	CMGC	*	*	*
DYRK4	CMGC	*	*	*
EEF2K	ATYPICAL	*	*	*
EGF-R	TK	***	****	****
EIF2AK2	OTHER	*	*	*
EIF2AK3	OTHER	*	*	*
EPHA1	TK	****	****	****
EPHA2	TK	****	****	****
EPHA3	TK	****	****	****
EPHA4	TK	****	****	****
EPHA5	TK	****	****	****
EPHA6	TK	*	***	***
EPHA7	TK	*	*	*
EPHA8	TK	****	****	****
EPHB1	TK	****	****	****
EPHB2	TK	****	****	****
EPHB3	TK	****	****	****
EPHB4	TK	****	****	****
ERBB2	TK	*	***	***
ERBB4	TK	****	****	****
ERK1	CMGC	*	*	*
ERK2	CMGC	*	*	*
ERK5	CMGC	*	*	*
ERK7	CMGC	*	*	*
FAK aa2-1052	TK	*	*	*
FER	TK	*	*	*
FES	TK	*	*	*
FGF-R1	TK	*	**	**
FGF-R2	TK	**	***	****
FGF-R3	TK	*	*	**
FGF-R4	TK	*	*	*
FGR	TK	****	****	****
FLT3	TK	***	*	**
FRK	TK	****	****	****
FYN	TK	****	****	****
GRK2	AGC	*	*	*
GRK3	AGC	*	*	*
GRK4	AGC	*	*	*
GRK5	AGC	*	*	*
GRK6	AGC	*	*	*
GRK7	AGC	*	*	*

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
GSG2	OTHER	*	*	*
GSK3-alpha	CMGC	*	*	*
GSK3-beta	CMGC	*	*	*
HCK	TK	****	****	****
HIPK1	CMGC	*	*	*
HIPK2	CMGC	*	*	*
HIPK3	CMGC	*	*	*
HIPK4	CMGC	*	*	*
HRI	OTHER	*	*	*
IGF1-R	TK	*	*	*
IKK-alpha	OTHER	*	*	*
IKK-beta	OTHER	*	*	*
IKK-epsilon	OTHER	*	*	**
INS-R	TK	*	*	*
INSR-R	TK	*	*	*
IRAK1	TKL	*	*	*
IRAK4 (untagged)	TKL	*	*	**
ITK	TK	*	*	*
JAK1 aa583-1154 wt	TK	*	***	***
JAK2	TK	**	**	**
JAK3	TK	*	*	**
JNK1	CMGC	*	*	*
JNK2	CMGC	*	*	*
JNK3	CMGC	*	*	*
KIT	TK	****	****	****
LCK	TK	****	****	****
LIMK1	TKL	*	*	*
LIMK2	TKL	*	*	*
LRRK2	TKL	*	*	**
LTK	TK	*	*	*
LYN	TK	****	****	****
MAP3K1	STE	*	*	*
MAP3K10	STE	*	**	***
MAP3K11	STE	**	***	****
MAP3K7/MAP3K7IP1	STE	*	*	*
MAP3K9	STE	*	**	***
MAP4K2	STE	*	*	*
MAP4K4	STE	*	*	*
MAP4K5	STE	***	****	****
MAPKAPK2	CAMK	*	*	*
MAPKAPK3	CAMK	*	*	*
MAPKAPK5	CAMK	*	*	*

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
MARK1	CAMK	*	*	*
MARK2	CAMK	*	*	*
MARK3	CAMK	*	*	*
MARK4	CAMK	*	*	*
MATK	TK	*	*	*
MEK1	STE	*	*	*
MEK2	STE	*	*	*
MEK5	STE	*	*	*
MEKK2	STE	*	**	***
MEKK3	STE	*	**	***
MELK	CAMK	*	*	*
MERTK	TK	*	*	*
MET	TK	*	*	*
MINK1	STE	*	**	**
MKK4	STE	*	*	*
MKK6 S207D/T211D##	STE	*	*	*
MKK7	STE	*	*	*
MKNK1	CAMK	**	*	*
MKNK2	CAMK	*	*	*
MLK4	TKL	*	*	*
MST1	STE	*	*	*
MST2	STE	*	*	*
MST3	STE	*	*	*
MST4	STE	*	*	***
mTOR	ATYPICAL	*	*	*
MUSK	TK	*	*	*
MYLK	CAMK	*	*	*
MYLK2	CAMK	*	*	**
MYLK3	CAMK	*	*	*
NEK1	OTHER	*	*	*
NEK11	OTHER	*	**	*****
NEK2	OTHER	*	*	*
NEK3	OTHER	*	*	*
NEK4	OTHER	*	*	*
NEK6	OTHER	*	*	*
NEK7	OTHER	*	*	*
NEK9	OTHER	*	*	*
NIK	STE	*	*	*
NLK	CMGC	***	****	*****
p38-alpha	CMGC	***	****	*****
p38-beta	CMGC	**	****	*****
p38-delta	CMGC	*	*	*

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
p38-gamma	CMGC	*	*	*
PAK1	STE	*	*	*
PAK2	STE	*	*	*
PAK3	STE	*	*	*
PAK4	STE	*	*	*
PAK6	STE	*	*	*
PAK7	STE	*	*	*
PASK	CAMK	*	*	*
PBK	OTHER	*	*	*
PDGFR-alpha	TK	****	****	****
PDGFR-beta	TK	****	****	****
PDK1	AGC	*	*	*
PHKG1	CAMK	*	*	*
PHKG2	CAMK	*	*	*
PIM1	CAMK	*	*	*
PIM2	CAMK	*	*	*
PIM3	CAMK	*	*	*
PKA	AGC	*	**	*
PKC-alpha	AGC	*	*	*
PKC-beta1	AGC	*	*	*
PKC-beta2	AGC	*	*	*
PKC-delta	AGC	*	*	*
PKC-epsilon	AGC	*	*	*
PKC-eta	AGC	*	*	*
PKC-gamma	AGC	*	*	*
PKC-iota	AGC	*	*	*
PKC-mu	AGC	*	*	*
PKC-nu	AGC	*	*	*
PKC-theta	AGC	*	*	**
PKC-zeta	AGC	*	*	*
PKMYT1	OTHER	*	*	*
PLK1	OTHER	*	*	*
PLK3	OTHER	*	*	*
PRK1	AGC	*	*	*
PRK2	AGC	*	*	*
PRKD2	CAMK	*	*	*
PRKG1	AGC	*	*	*
PRKG2	AGC	*	*	*
PRKX	AGC	*	*	**
PYK2	TK	*	*	*
RAF1 Y340D/Y341D (untagged)##	TKL	***	****	****
RET	TK	*	***	****

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
RIPK2	TKL	****	****	****
RIPK5	TKL	*	*	*
ROCK1	AGC	*	*	*
ROCK2	AGC	*	*	*
RON	TK	*	*	*
ROS	TK	*	*	*
RPS6KA1	AGC	*	*	*
RPS6KA2	AGC	*	*	**
RPS6KA3	AGC	*	*	*
RPS6KA4	AGC	*	*	*
RPS6KA5	AGC	*	*	*
RPS6KA6	AGC	*	*	****
S6K	AGC	*	*	*
S6K-beta	AGC	*	*	*
SAK	OTHER	*	*	*
SGK1	AGC	*	*	*
SGK2	AGC	*	*	*
SGK3	AGC	*	*	*
SIK1	CAMK	****	****	****
SIK2	CAMK	****	****	****
SIK3	CAMK	****	****	****
SLK	STE	*	**	**
SNARK	CAMK	*	*	*
SNK	OTHER	*	*	*
SRC (GST-HIS-tag)	TK	****	****	****
SRMS	TK	***	****	****
SRPK1	CMGC	*	*	*
SRPK2	CMGC	*	*	*
STK17A	CAMK	*	*	*
STK23	CAMK	*	*	*
STK25	STE	*	*	**
STK33	CAMK	*	*	*
STK39	STE	*	*	*
SYK aa1-635	TK	*	**	**
TAOK2	STE	*	*	*
TAOK3	STE	*	*	*
TBK1	OTHER	*	*	***
TEC	TK	****	****	****
TGFB-R1	TKL	***	****	****
TGFB-R2	TKL	*	**	***
TIE2	TK	*	*	**
TLK1	AGC	*	*	*

FIGURE 3 (cont)

Kinase Name	Kinase Family	B3 (1μM)	A8 (1μM)	C7 (1μM)
TLK2	AGC	*	*	*
TNK1	TK	*	*	**
TRK-A	TK	**	**	***
TRK-B	TK	*	*	**
TRK-C	TK	**	**	***
TSF1	OTHER	*	*	*
TSK2	CAMK	*	*	*
TSSK1	CAMK	*	*	*
TTBK1	CK1	*	*	*
TTBK2	CK1	*	*	*
TTK	OTHER	*	*	*
TXK	TK	****	****	****
TYK2	TK	*	*	*
TYRO3	TK	*	*	*
VEGF-R1	TK	*	*	**
VEGF-R2	TK	*	**	**
VEGF-R3	TK	*	*	**
VRK1	CK1	*	*	*
VRK2	CK1	*	*	**
WEE1	OTHER	*	**	***
WNK1	OTHER	*	*	*
WNK2	OTHER	*	**	***
WNK3	OTHER	*	*	**
YES	TK	****	****	****
ZAK	TKL	****	****	****
ZAP70	TK	*	*	*
Selectivity Score	< 50 % residual activity	0.163	0.188	0.234

FIGURE 4

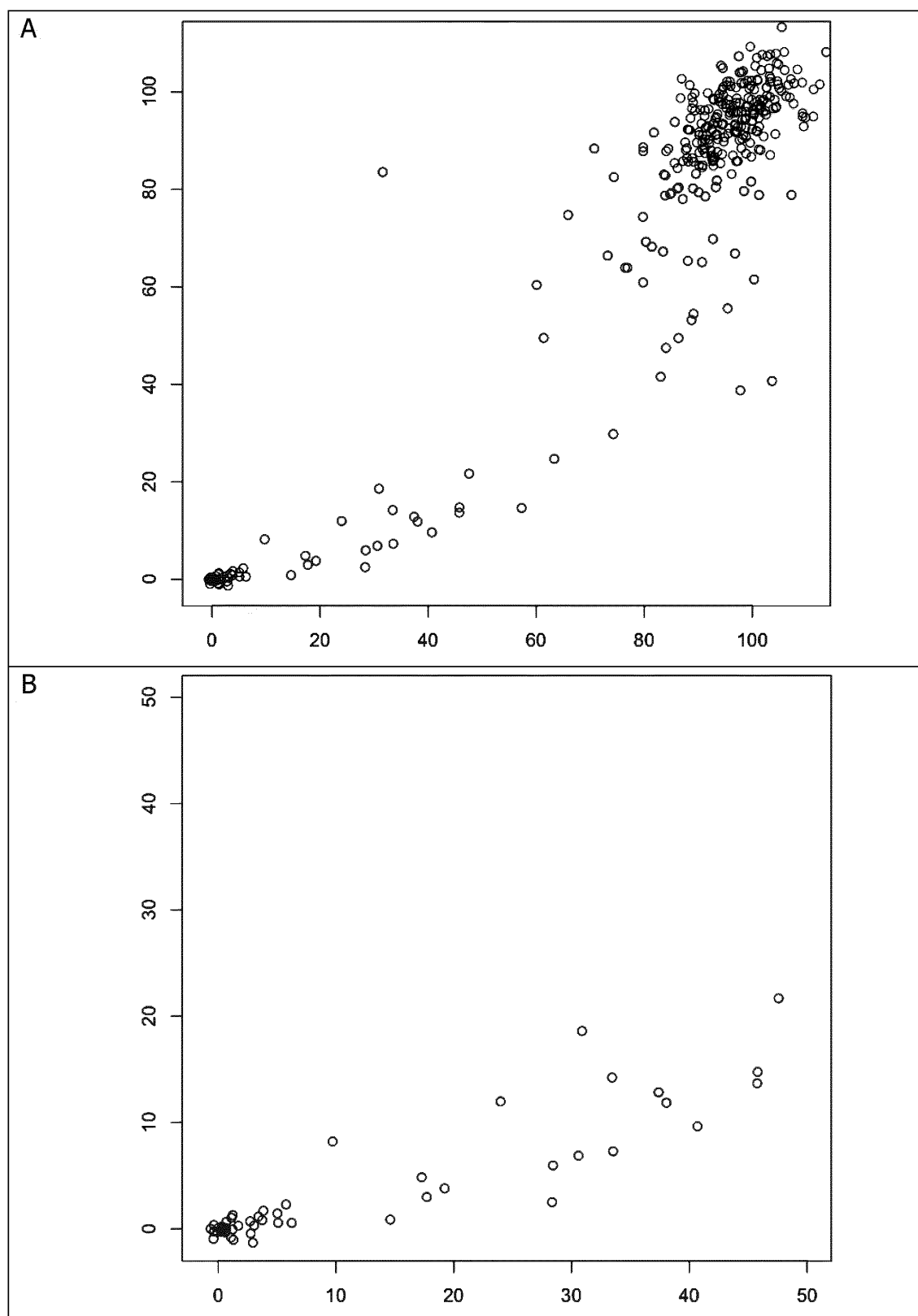


FIGURE 5

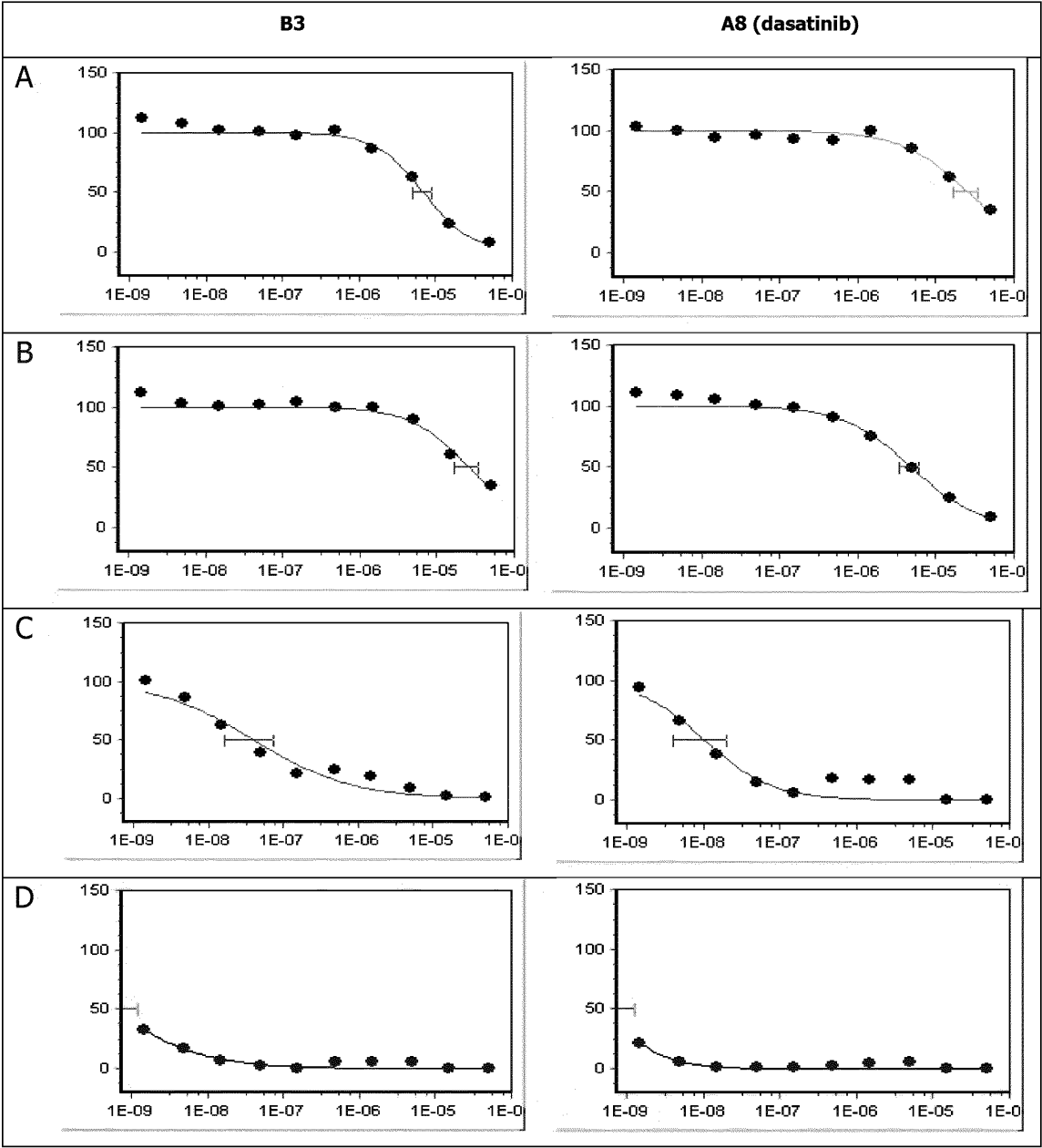


FIGURE 6

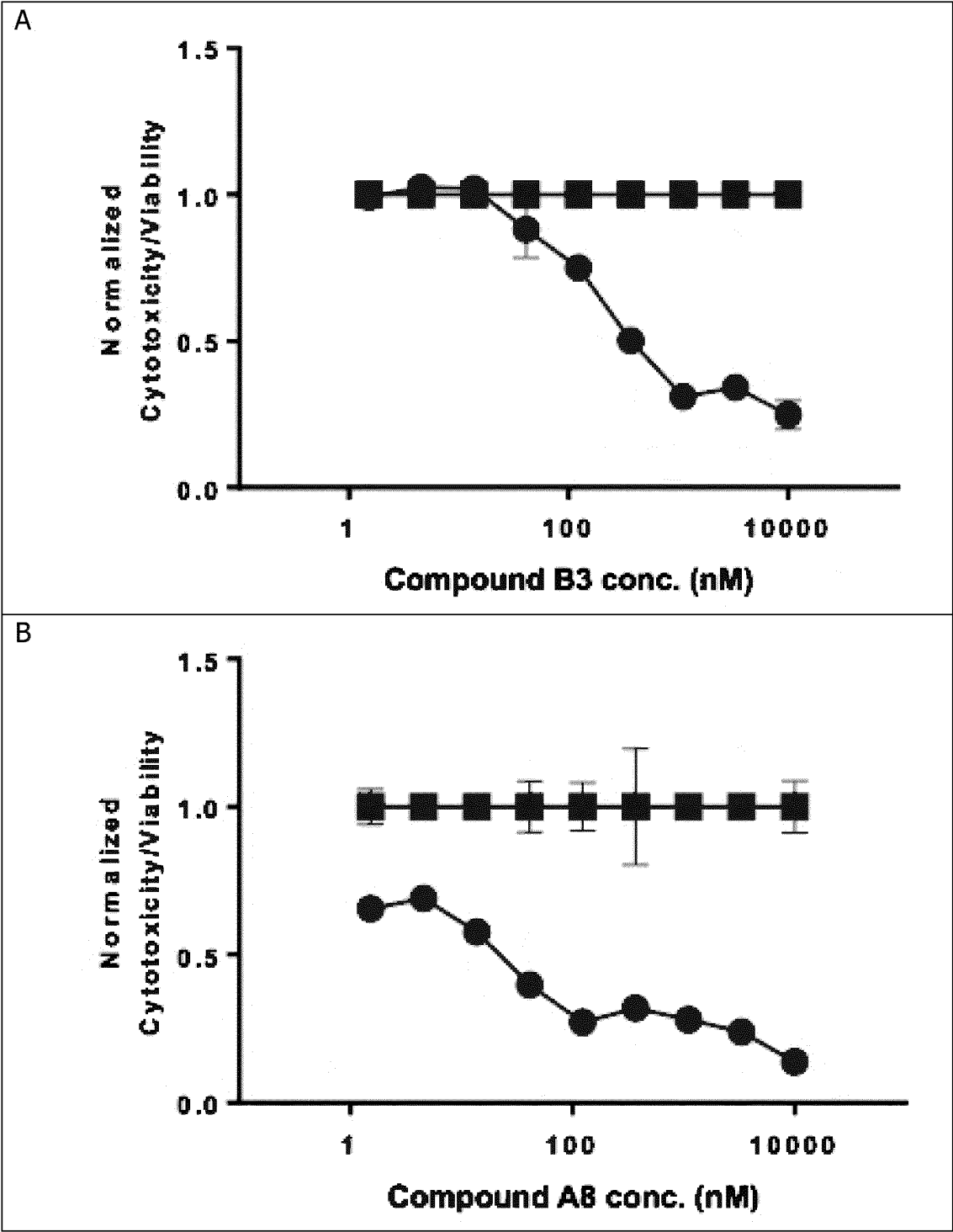


FIGURE 7

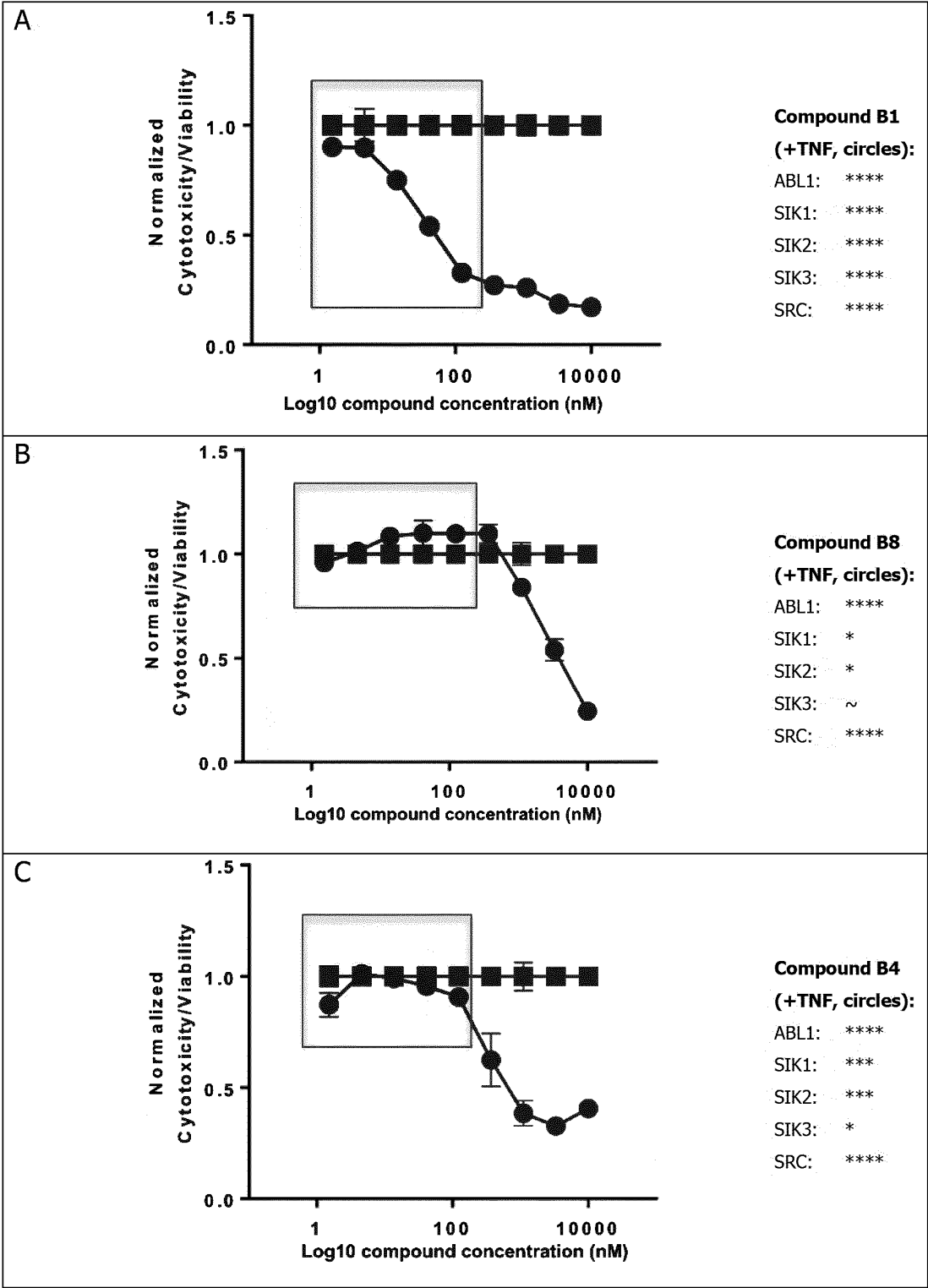
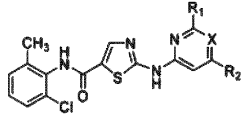


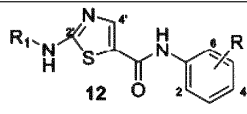
FIGURE 8

A



compd	X	R ₁	R ₂	IC ₅₀ ^a , nM			
				K562	PC3	MDA-MB-231	WiDr
1	N	CH ₃	CH ₃	1.6, 2.1	67		
2	CH		H	<3.0	2.8	<3.0	4.1
3	CH		H	<2.0	3.6 (2.1)	6.2	23
4	CH		H	<3.0	13 (8)	3.1, 5.4	7.9, 47
5	CH		H	<2.0	10	42, 34	32, 67
6	N	H		<3.0	24 (16)	45 (25)	270 (170)
7	N	H		<2.0	82	170	270
8	N	CH ₃		<3.0	3.6 (2.3)	16	27
9	N	CH ₃		<1.0	25	47	180
10	N	CH ₃		<2.0	14	23, 28	92, 27
11	N	CH ₃		<4.0	27 (25)	140	210 (120)
12	N	CH ₃		<1.0	11 (8)	9.0 (5.1)	41
13	N	CH ₃		<1.0	9.4 (5.6)	12 (10)	52 (38)

B



compd	R	R ₁	hLck IC ₅₀ ^a (nM)	T-cell IC ₅₀ ^b (nM)
12a	2-Cl, 6-Me	2''-pyridyl	1.2	140
12b	2-Cl, 6-Me	3''-pyridyl	6.7	870
12c	2-Cl, 6-Me	4''-pyridyl	9.4	270
12d	2,6-di-Me	2''-pyridyl	1.2	180
12e	2,4,6-tri-Me	2''-pyridyl	5	510
12f	2-Cl, 6-Me	3''-pyridazinyl	4	350
12g	2,6-di-Me	3''-pyridazinyl	0.3	350
12h	2-Cl, 6-Me	3'',5''-di-Me-2''-pyrazinyl	6.3	570
12i	2,4,6-tri-Me	2''-pyrazinyl	4.9	500
12j	2-Cl, 6-Me	6''-Me-2''-pyridinyl	0.6	110
12k	2-Cl, 6-Me	4''-Me-2''-pyridinyl	0.5	80
12l	2-Cl, 6-Me	4'',6''-di-Me-2''-pyridinyl	4	140
12m	2-Cl, 6-Me	2'',6''-di-Me-4''-pyrimidinyl	1	80
12n	2-Cl, 6-Me	4'',6''-di-Me-2''-pyrimidinyl	50	
12o	2,4,6-tri-Me	2'',6''-di-Me-4''-pyrimidinyl	3	140

^a n = 3, variation in individual values, <20%. ^b n = 3, variation in individual values, <30%.

FIGURE 9

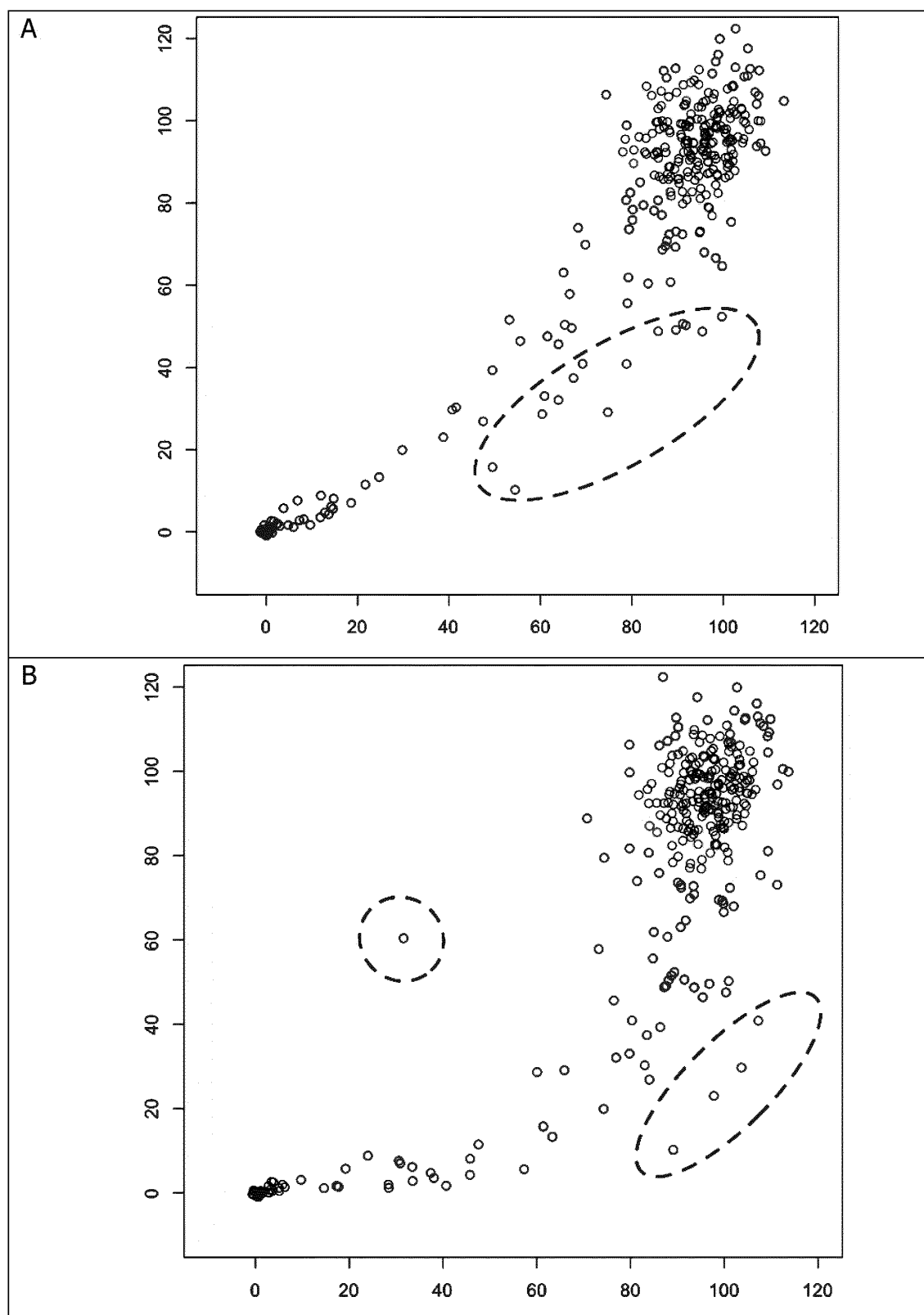


FIGURE 10

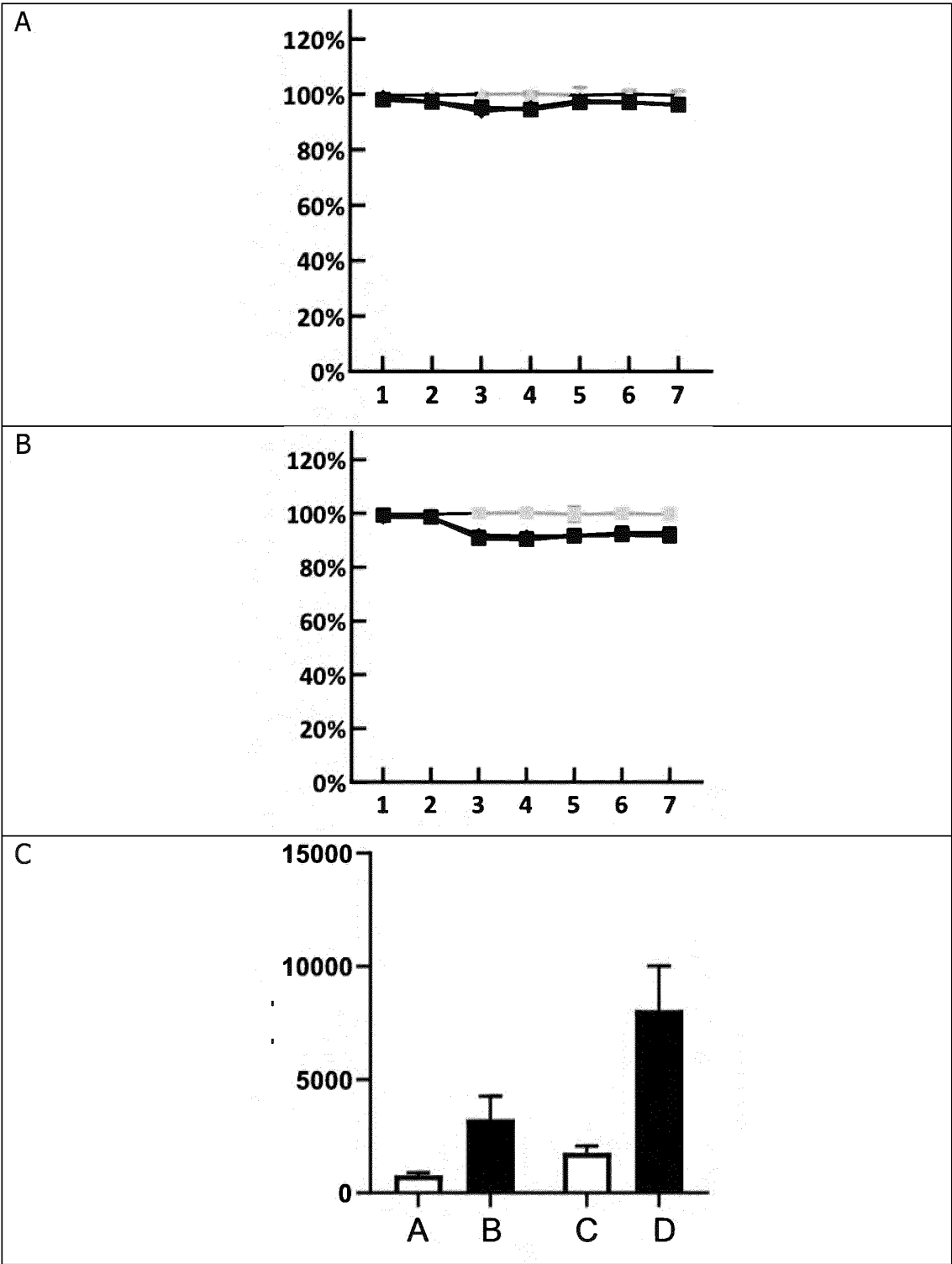


FIGURE 11

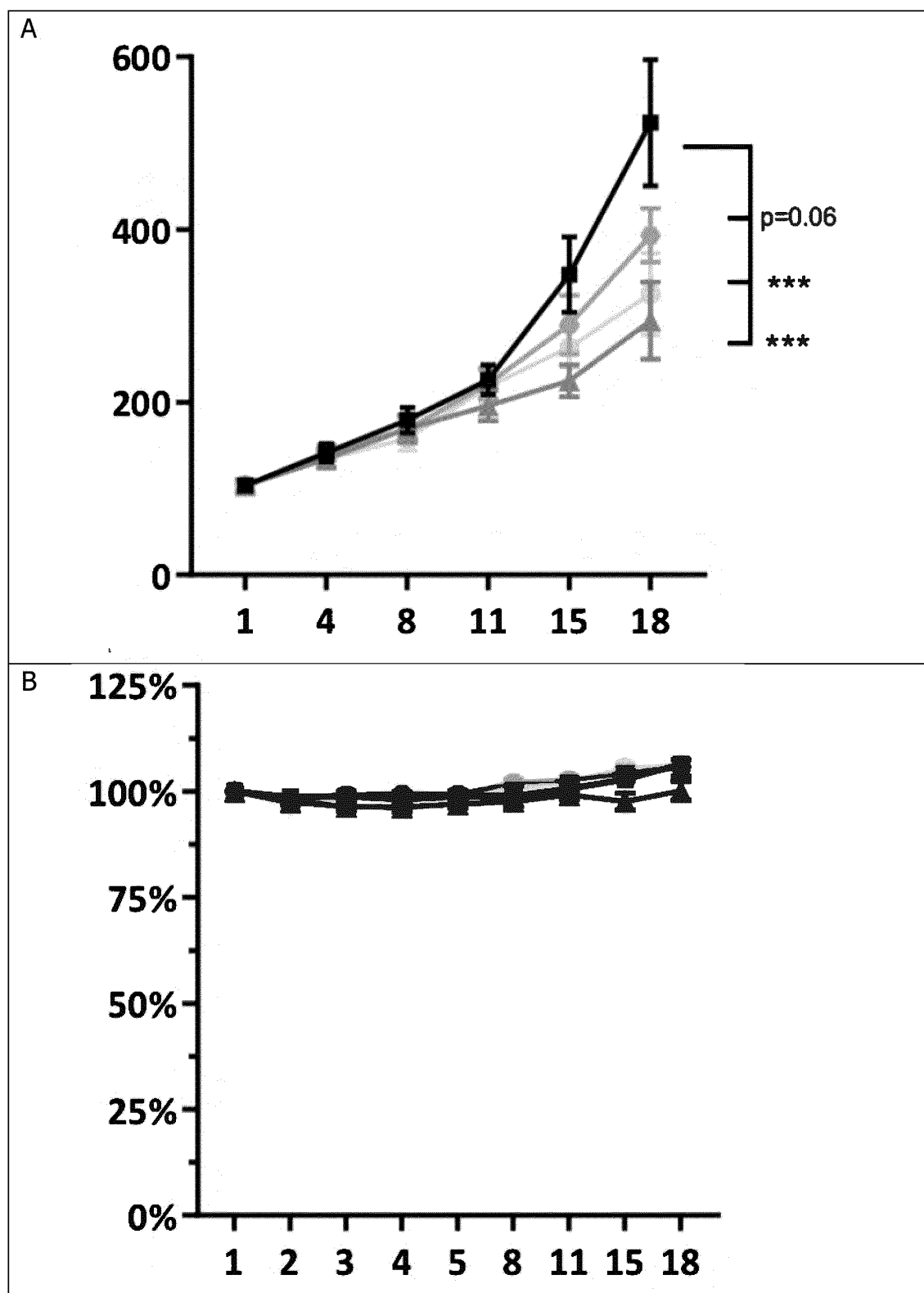


FIGURE 12

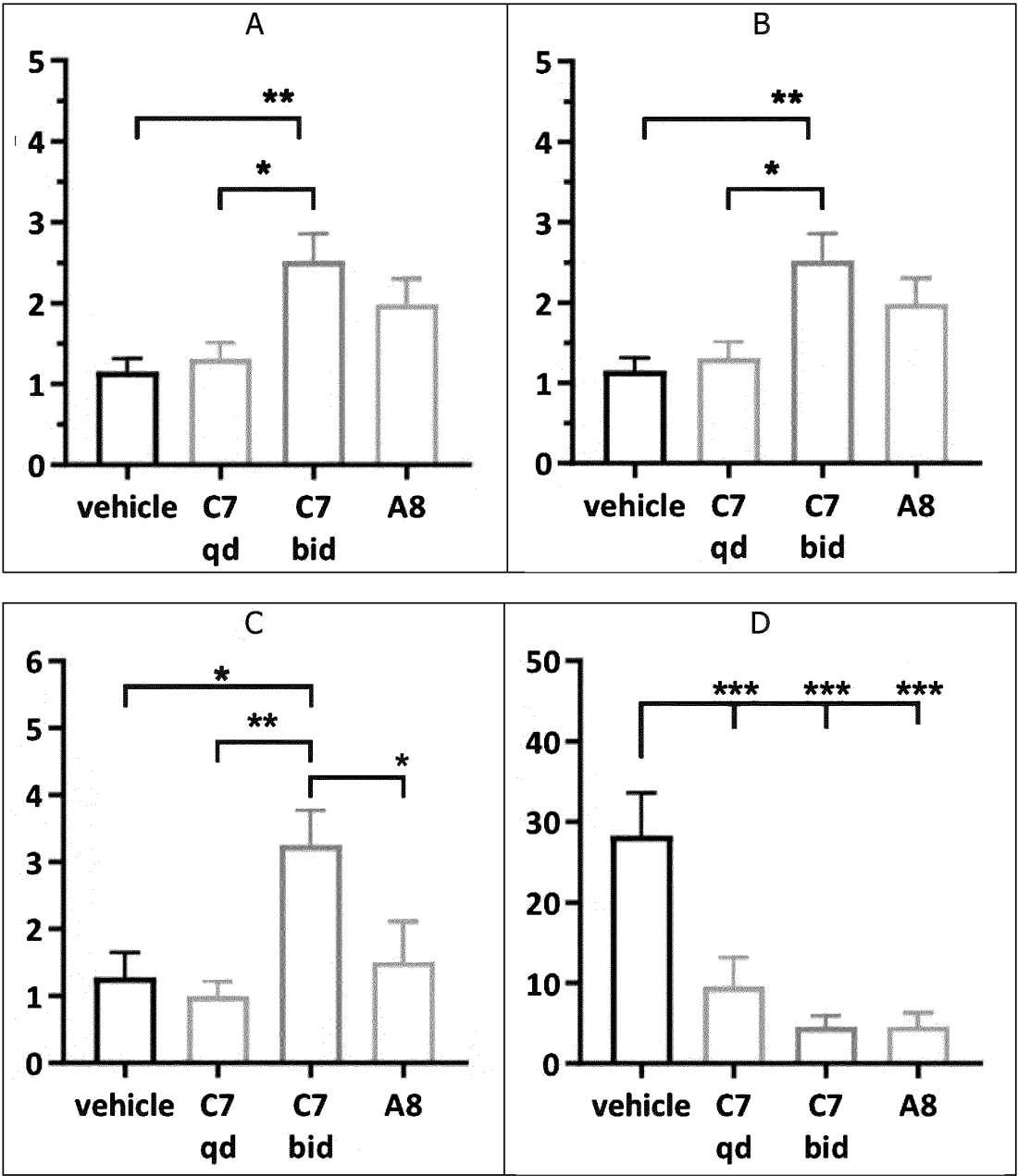


FIGURE 13

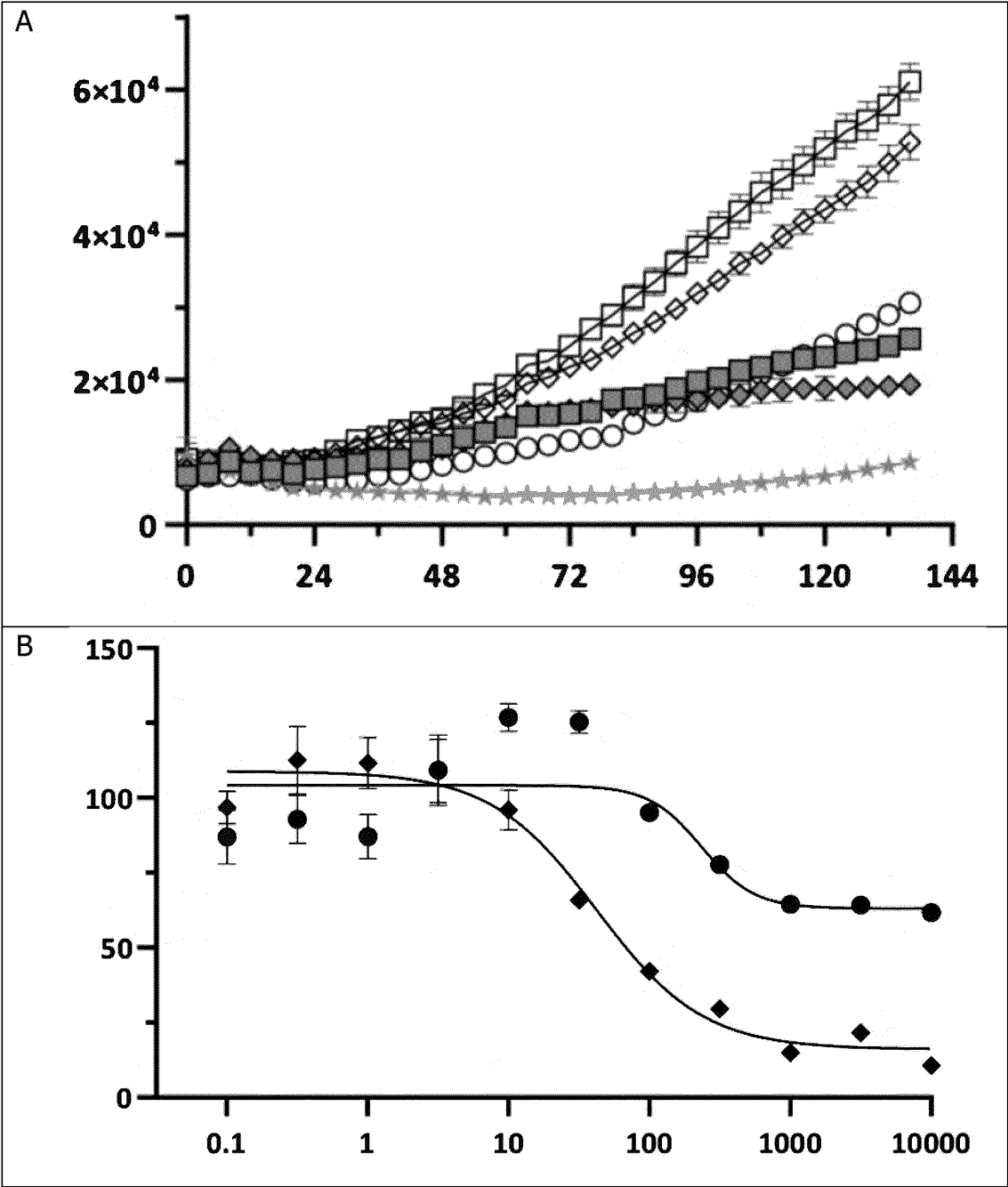


FIGURE 14

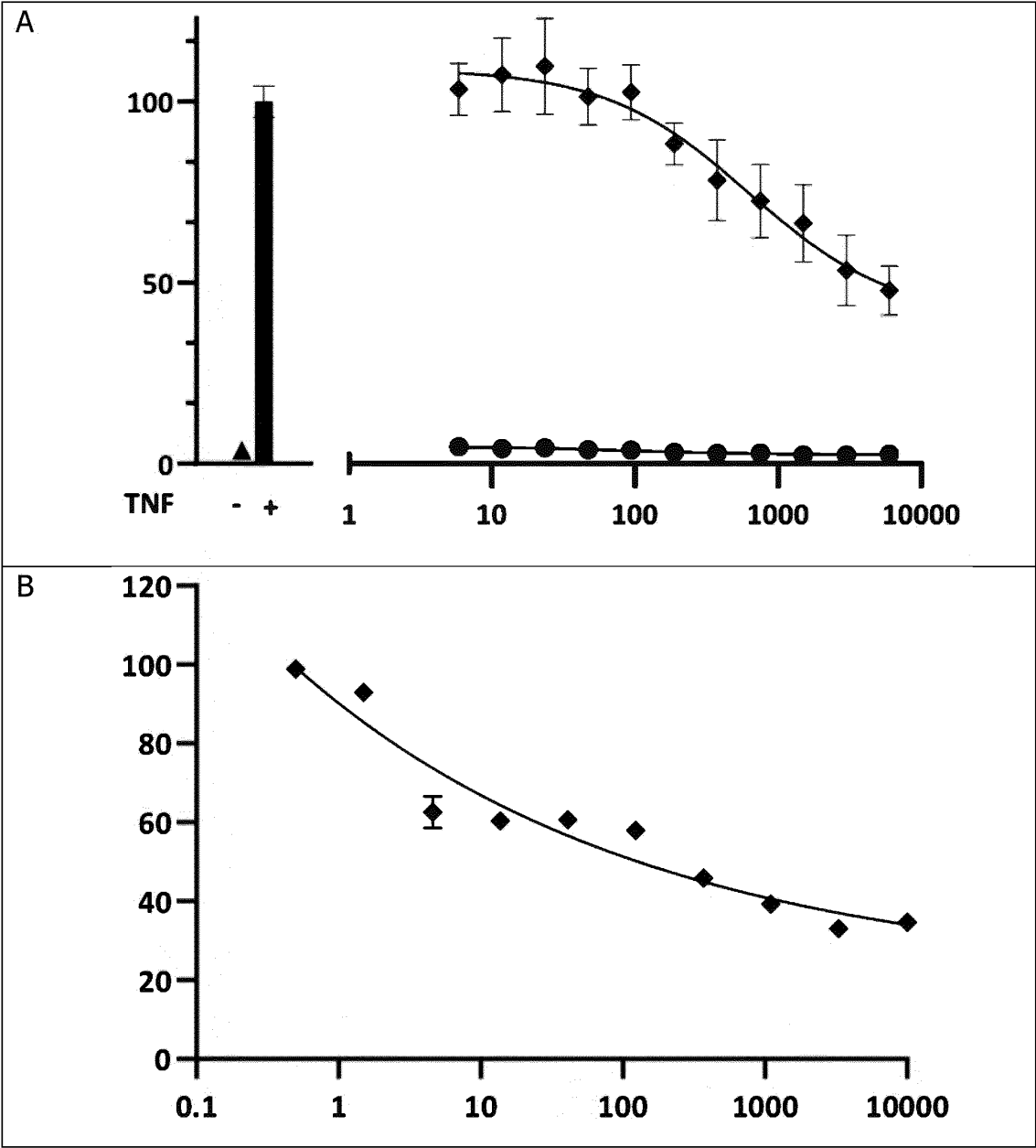


FIGURE 15

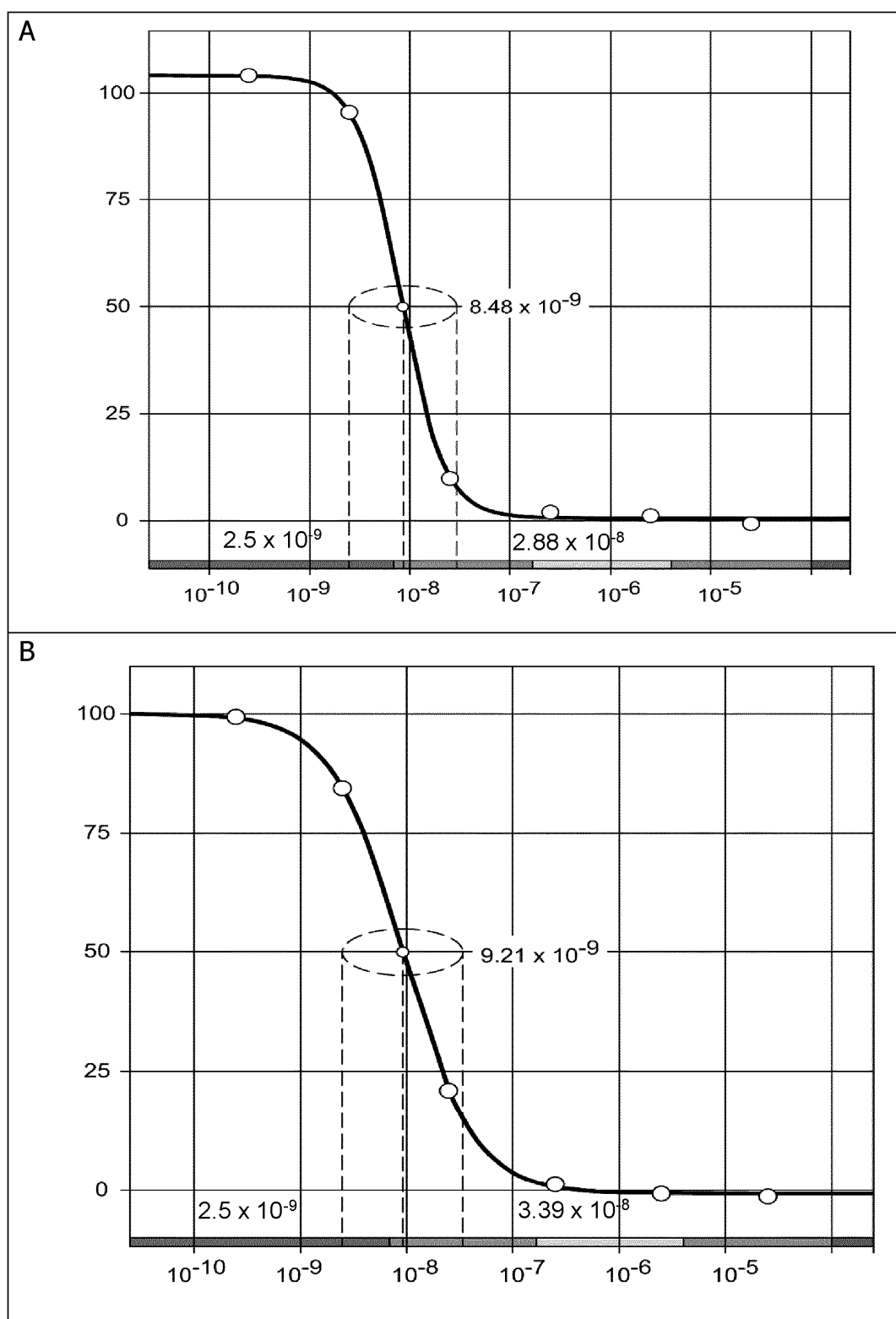


FIGURE 16

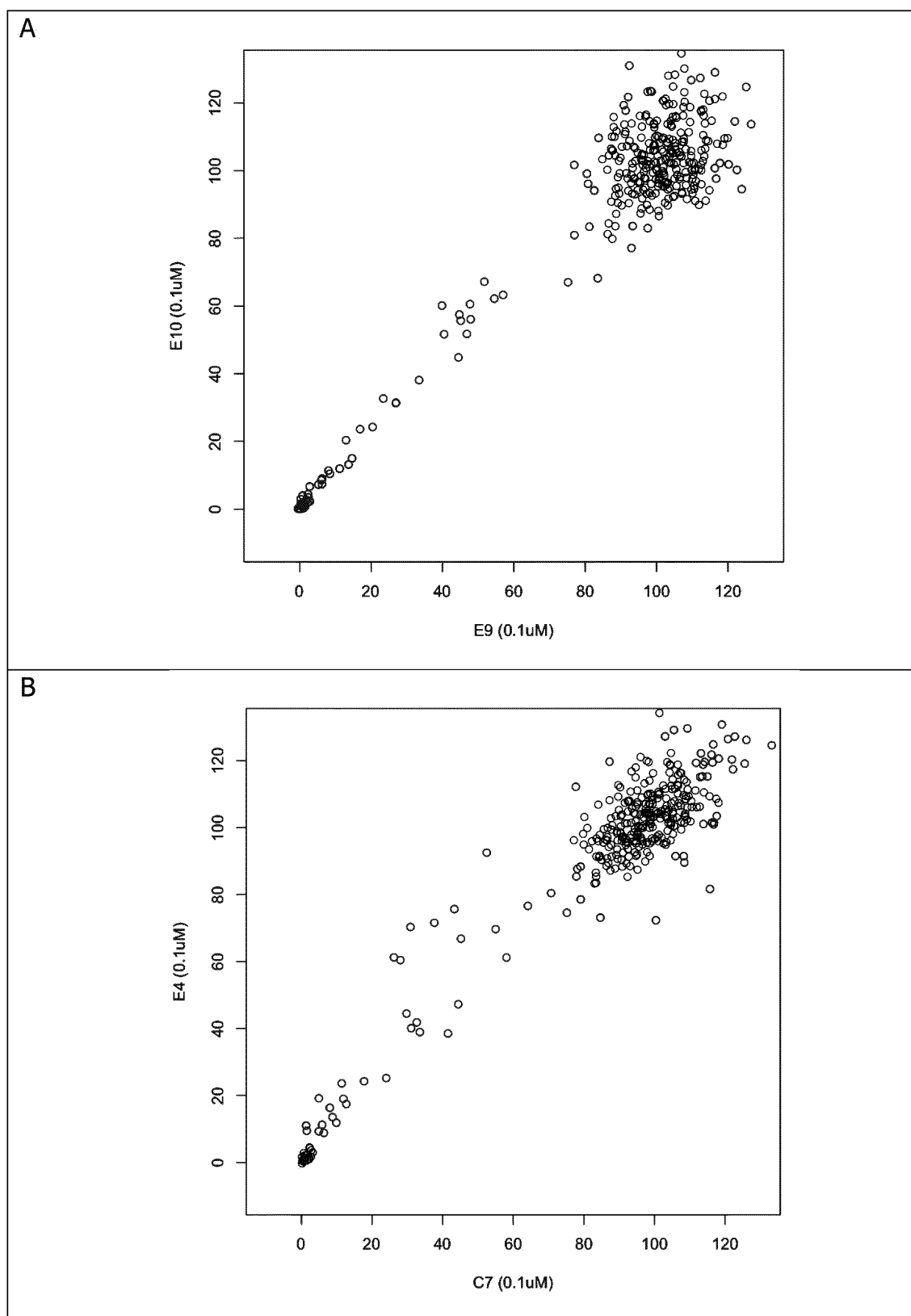


FIGURE 17

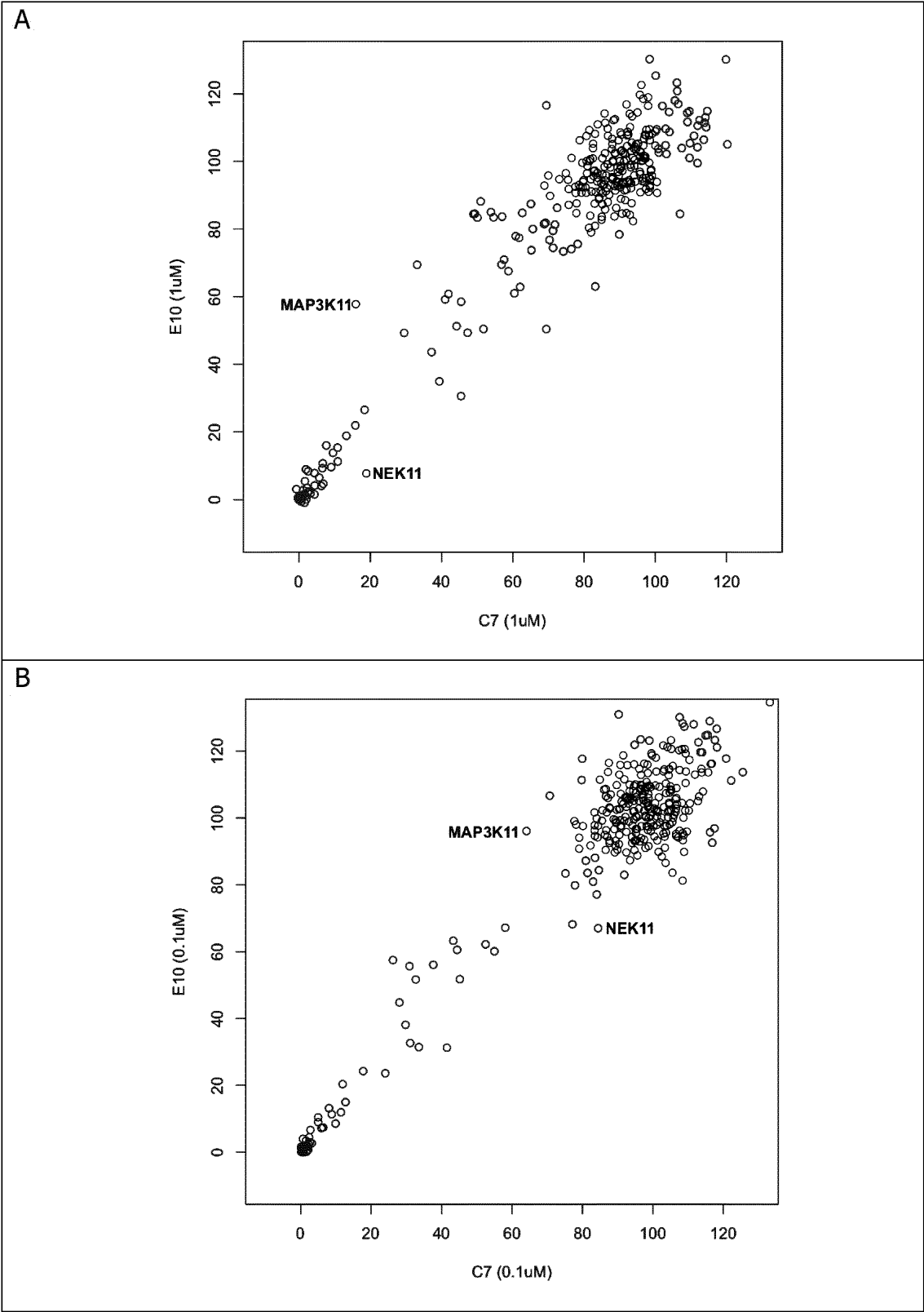


FIGURE 18

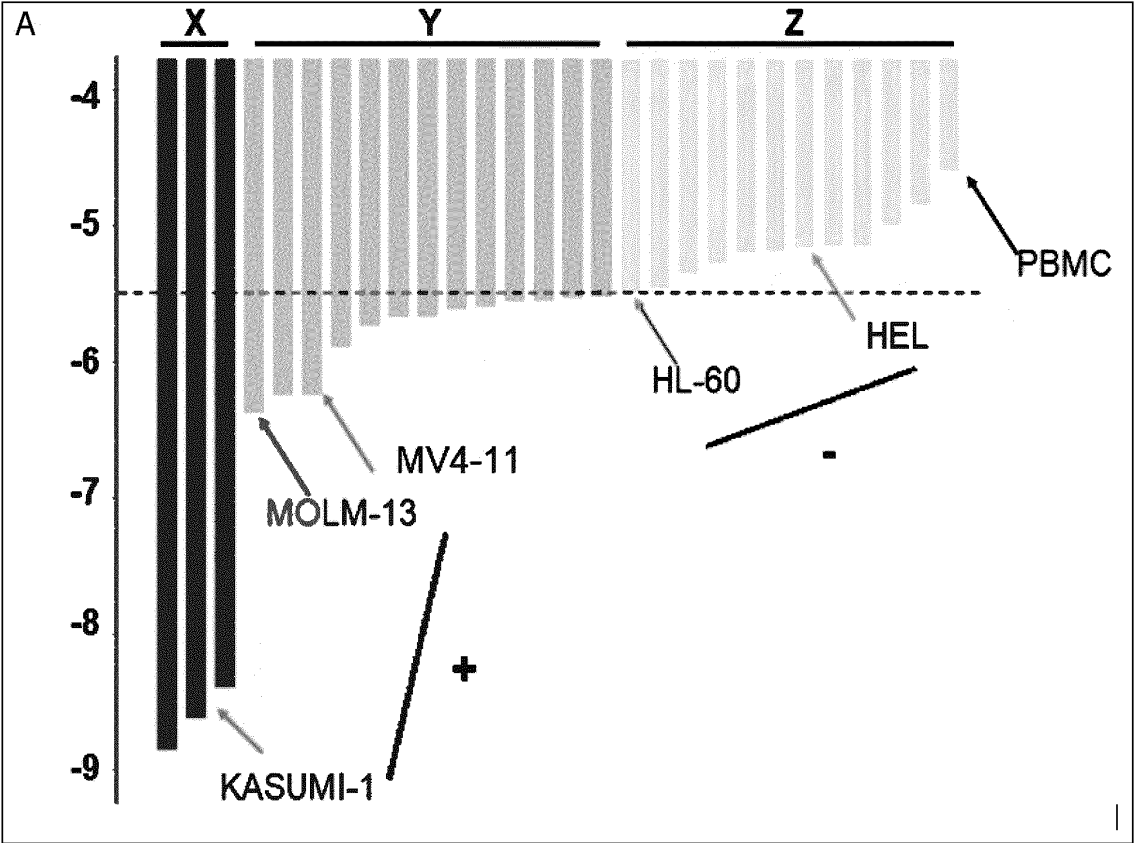


FIGURE 18 (CONT)

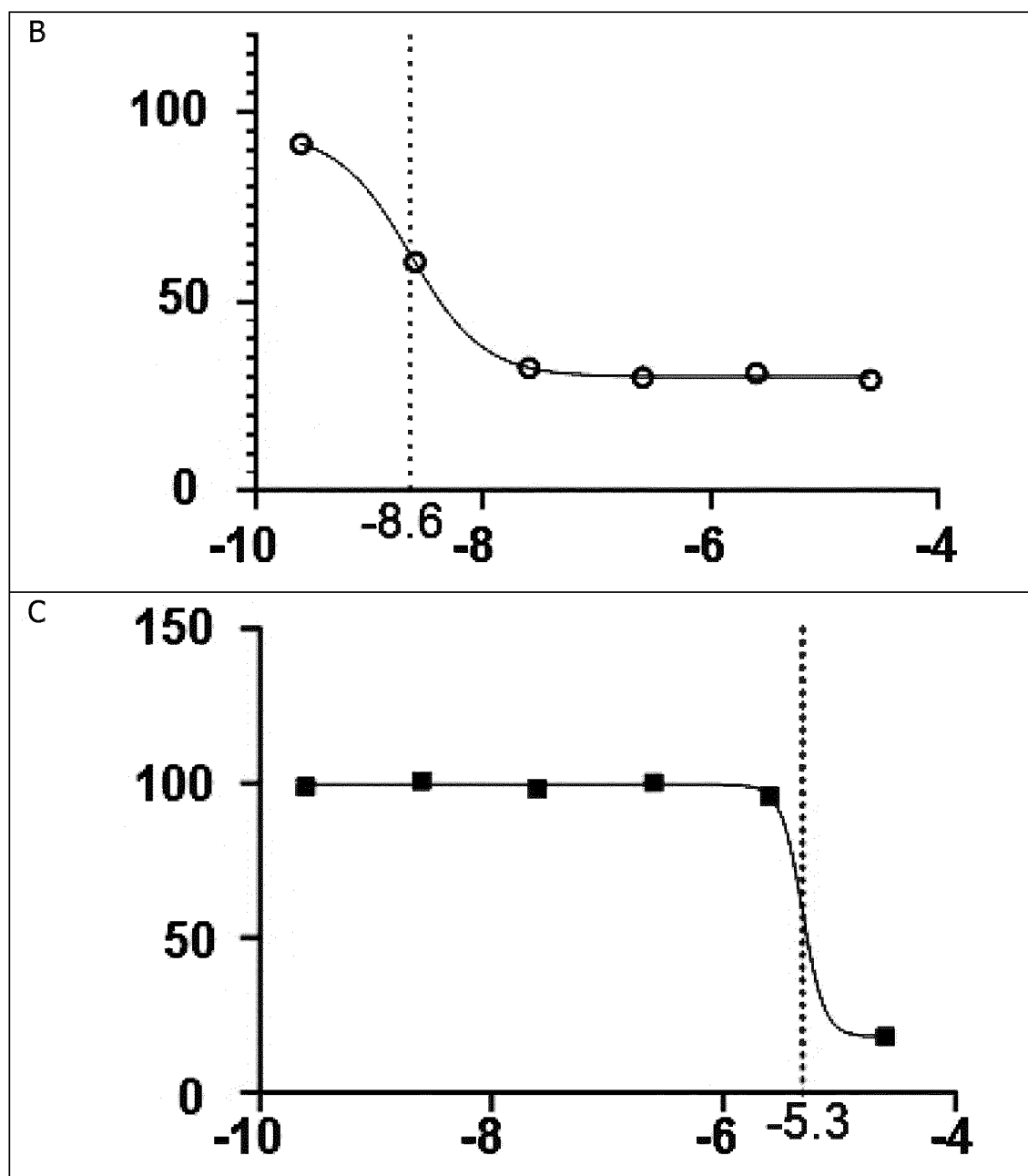


FIGURE 19

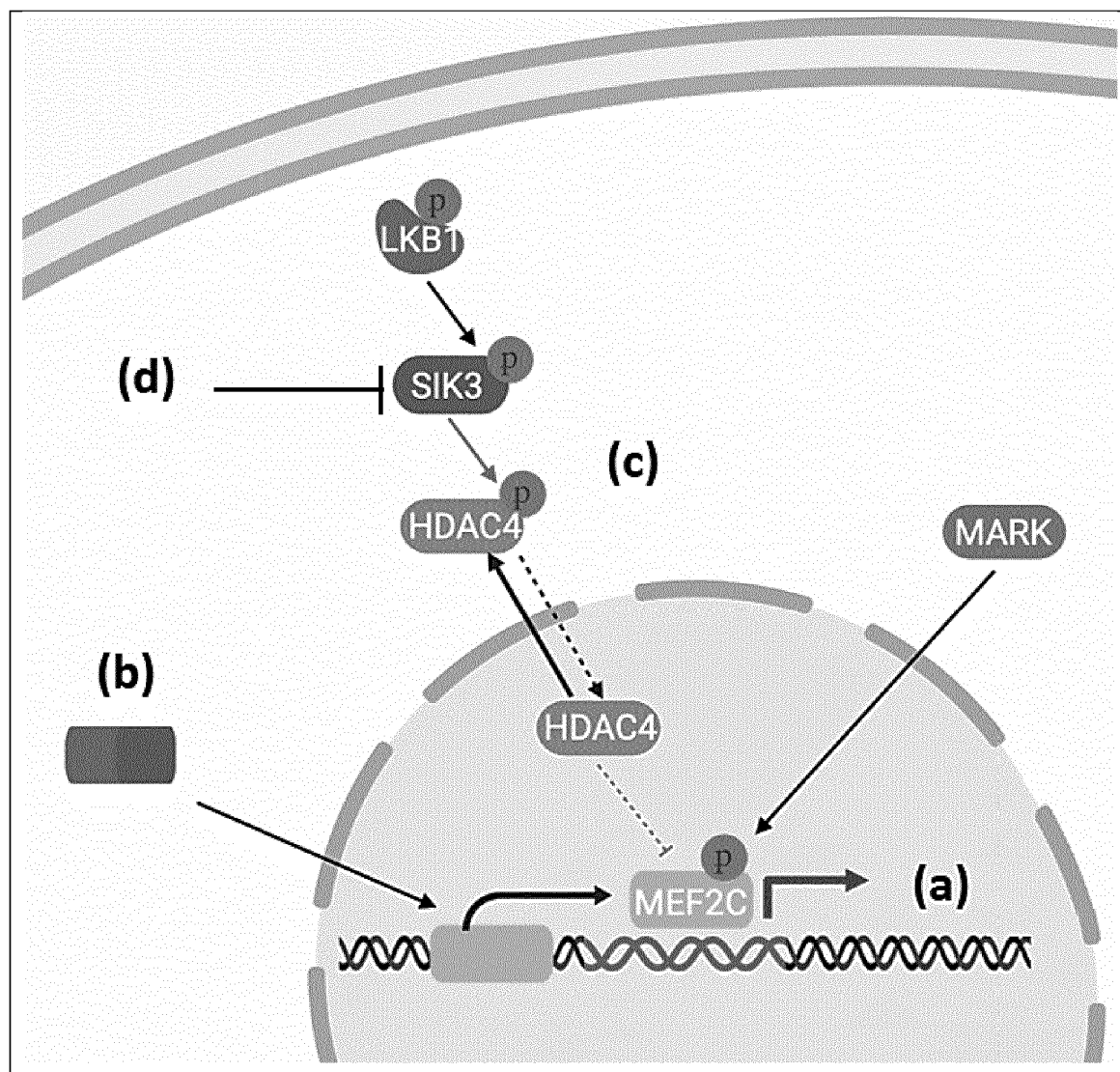


FIGURE 20

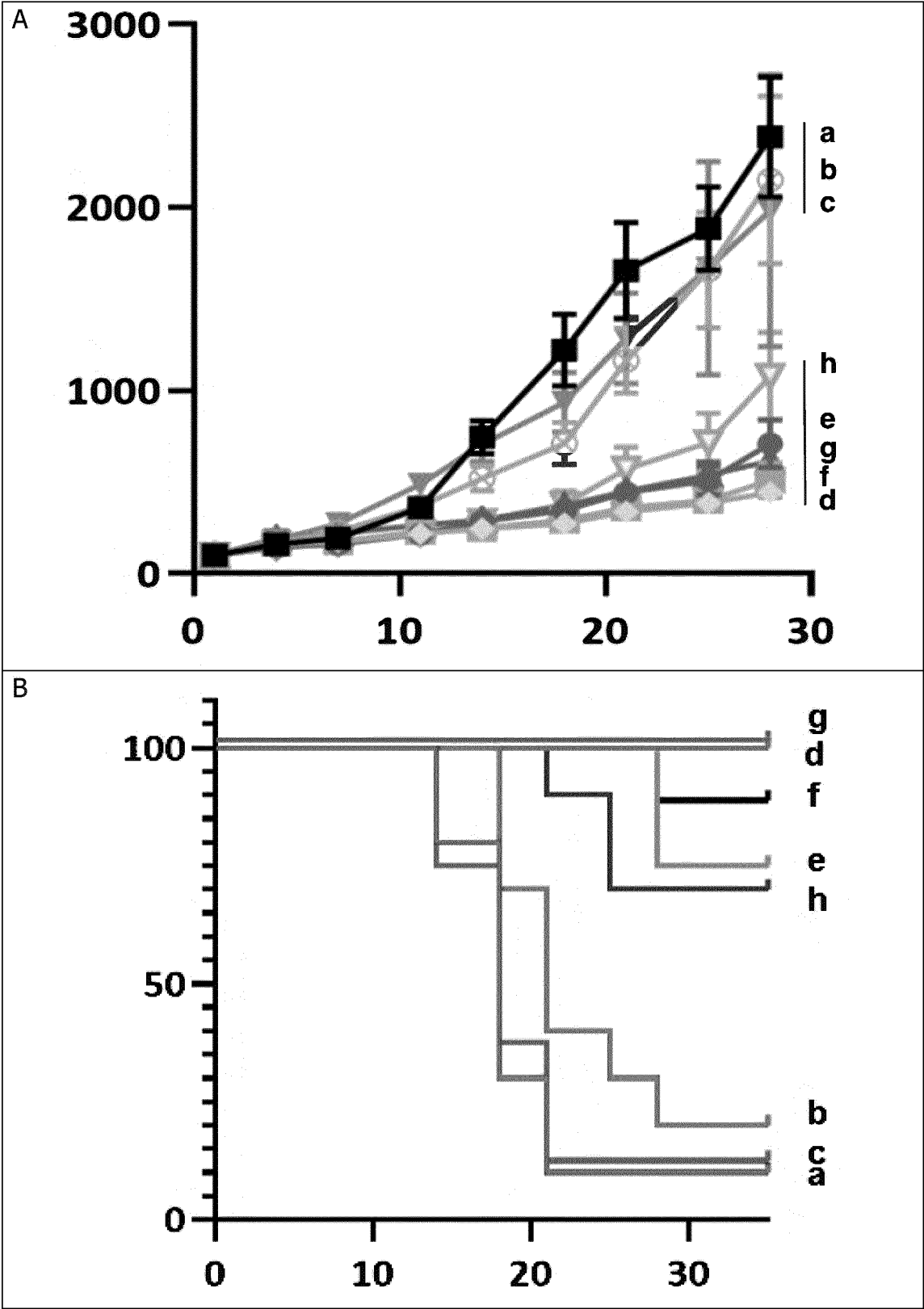


FIGURE 20 (cont)

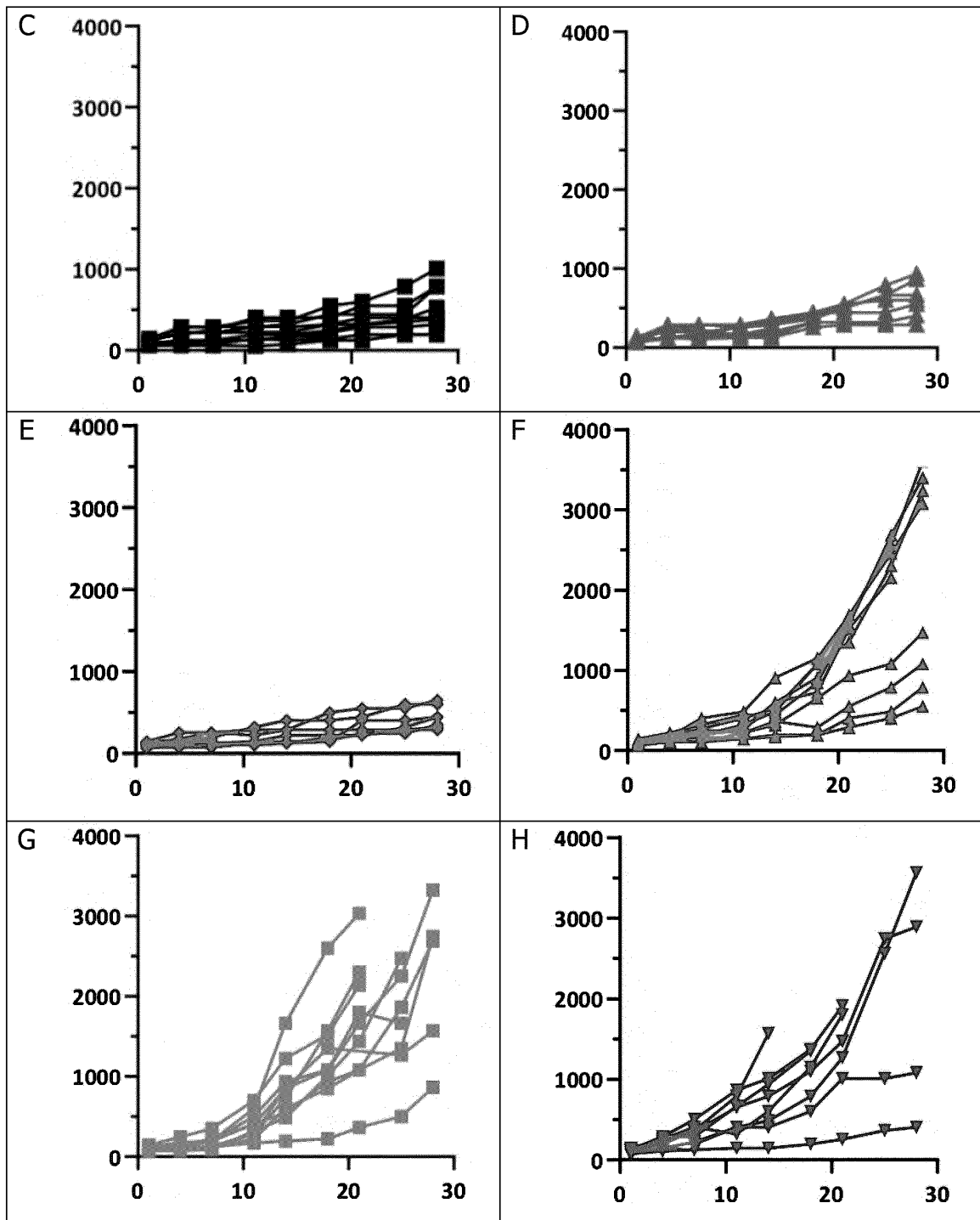


FIGURE 21

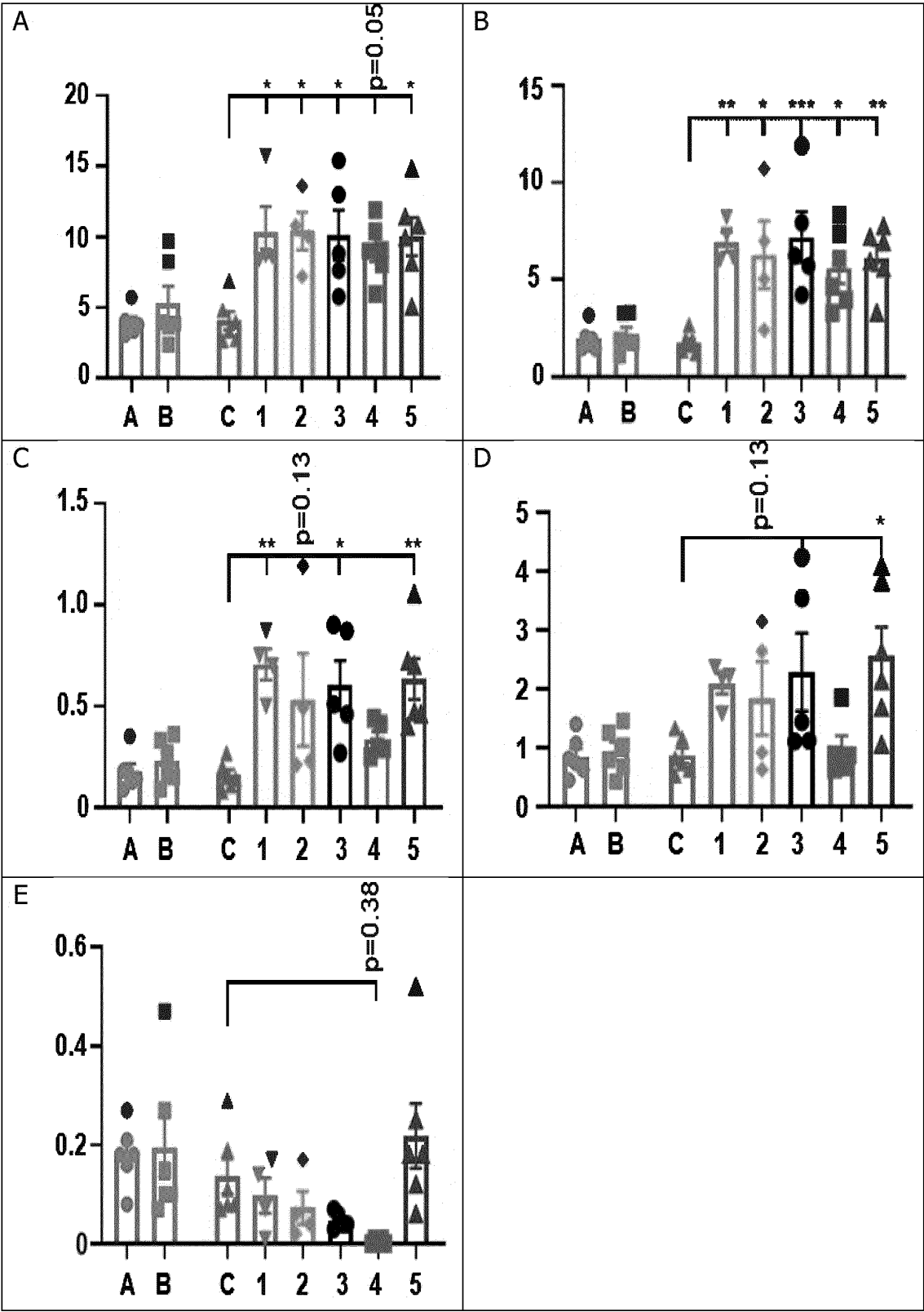


FIGURE 21 (cont)

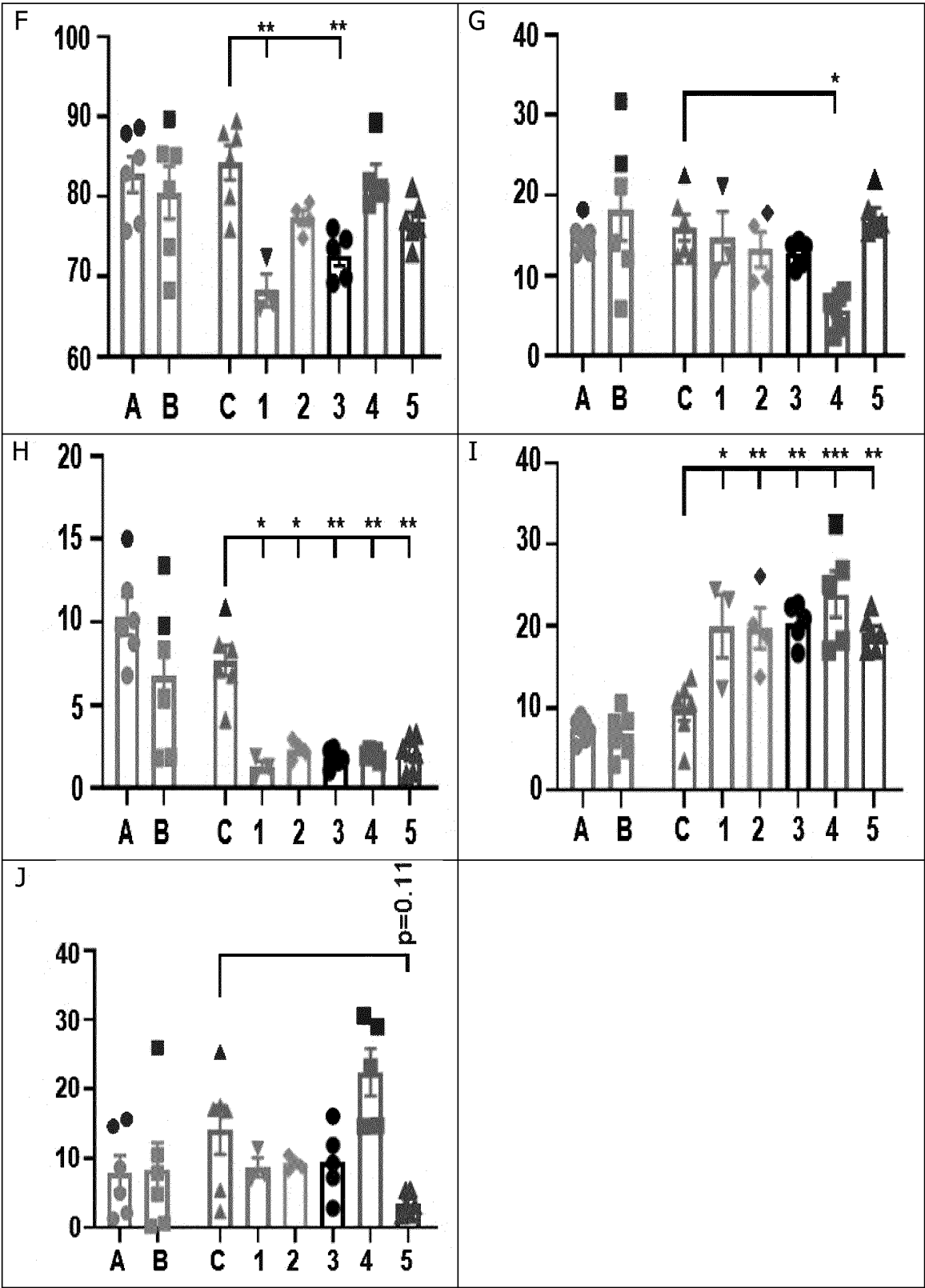


FIGURE 22

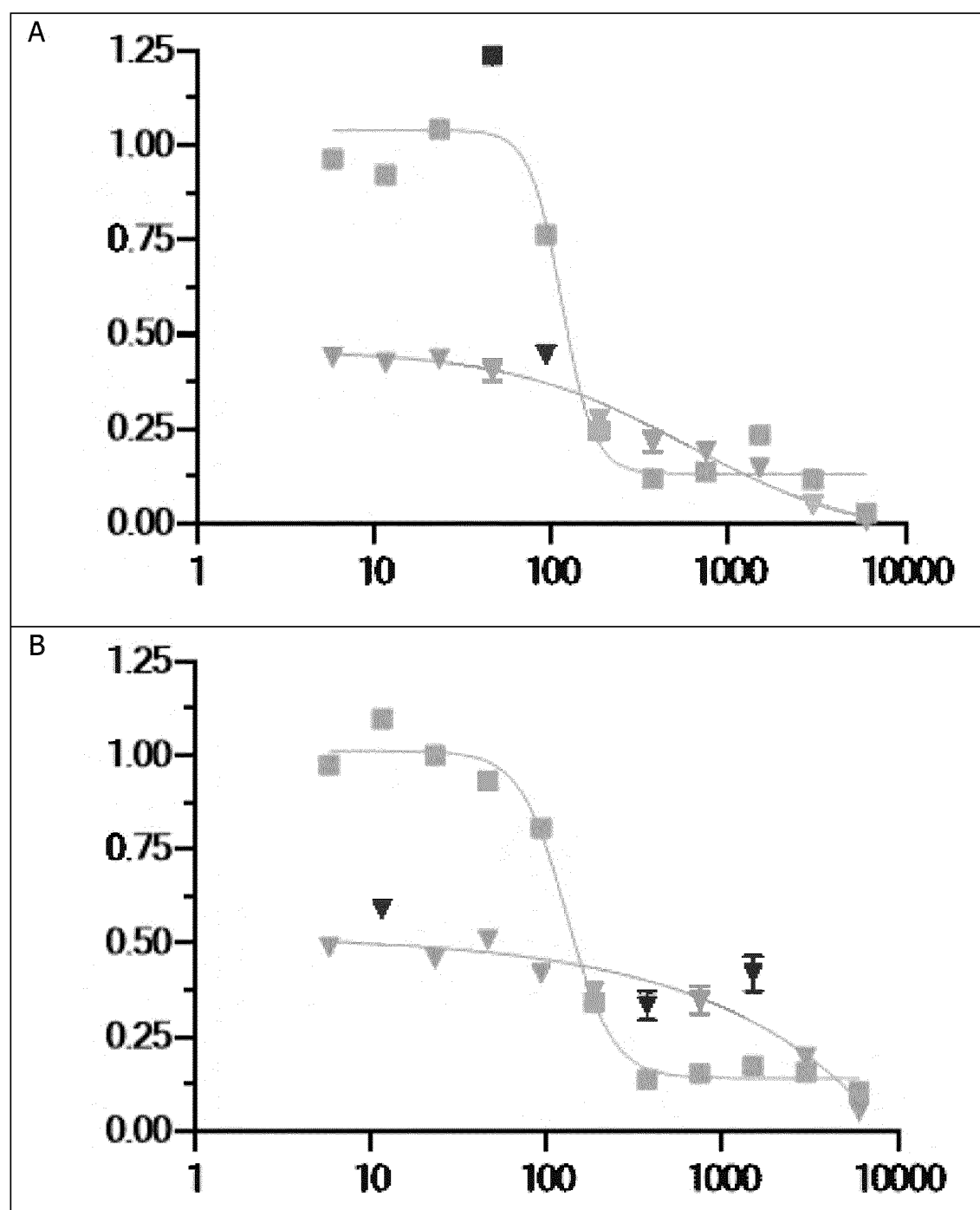


FIGURE 23

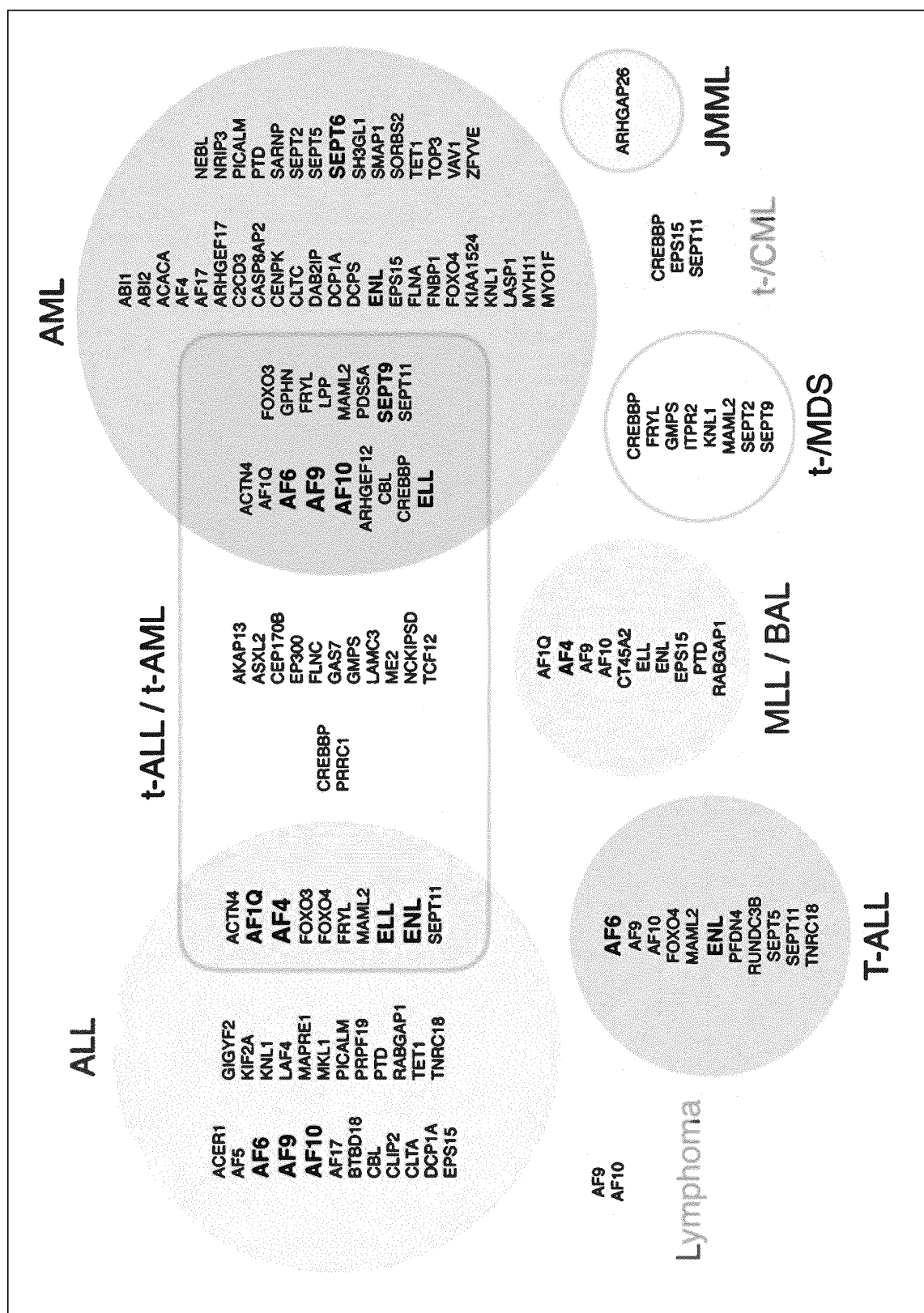


FIGURE 24

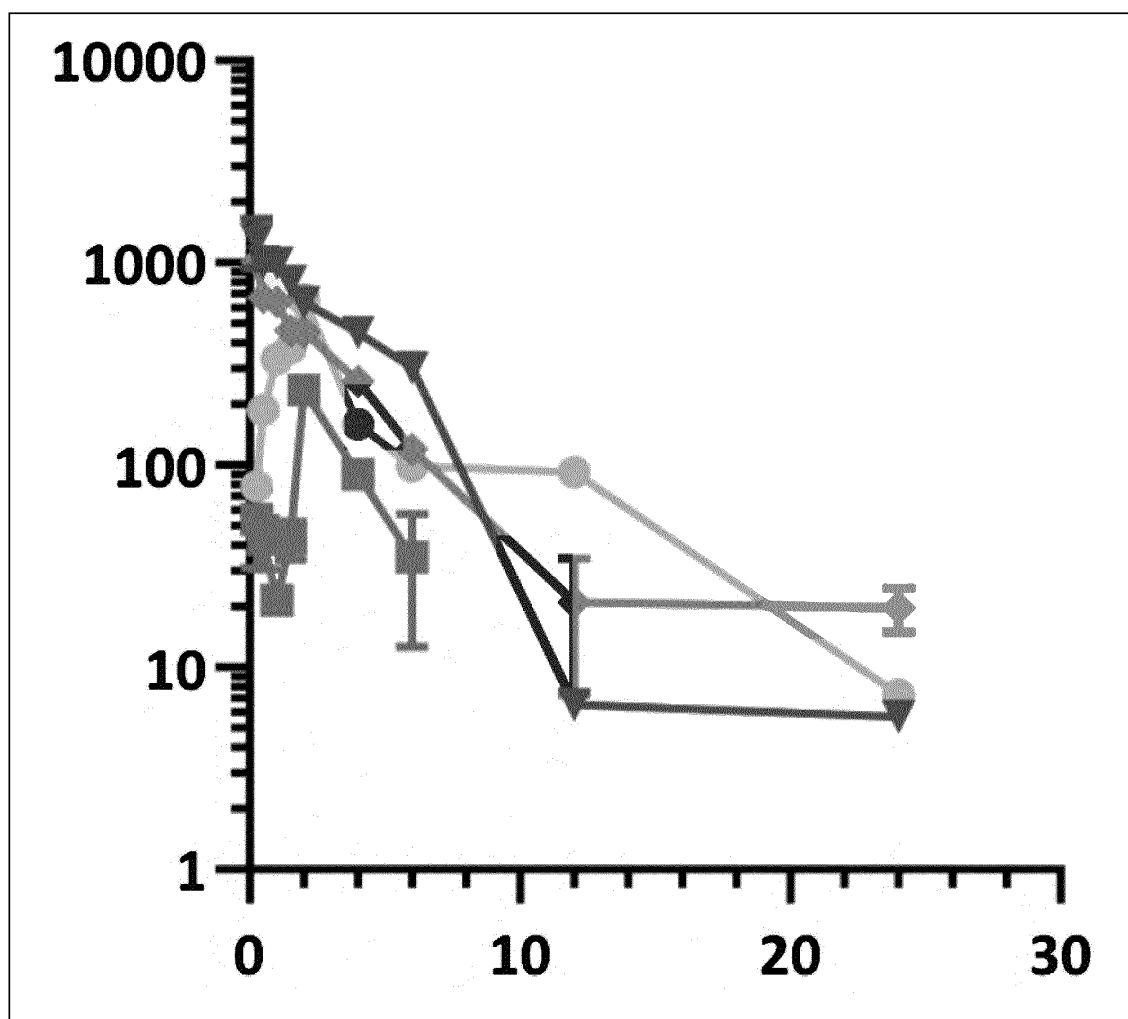


FIGURE 25

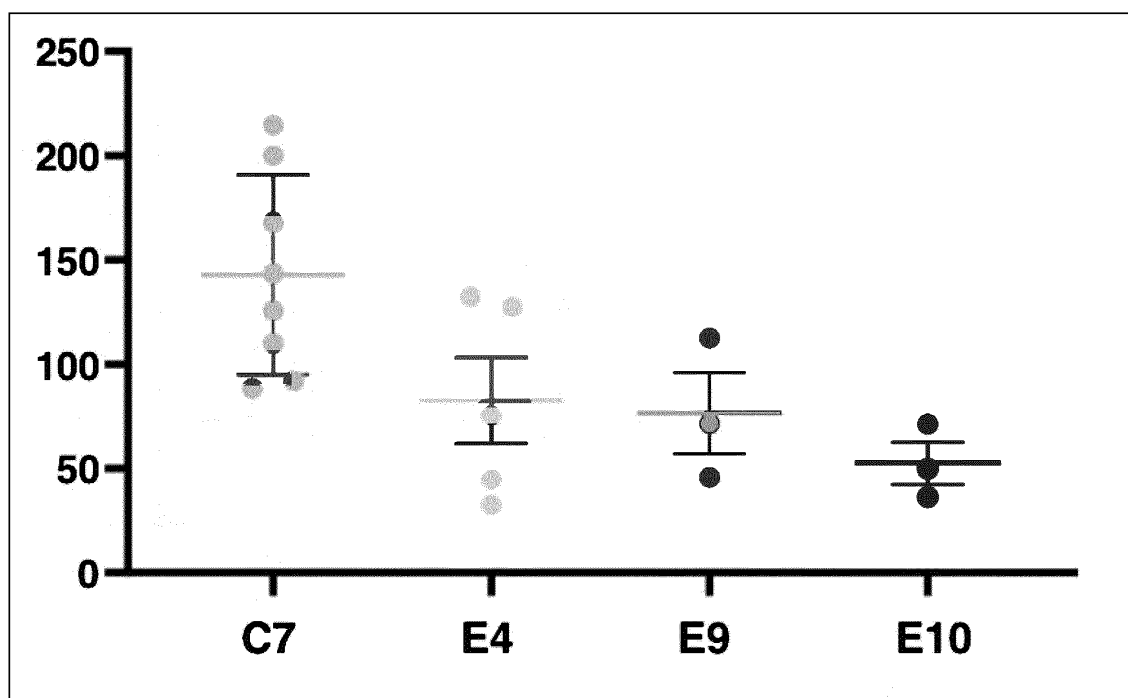


FIGURE 26

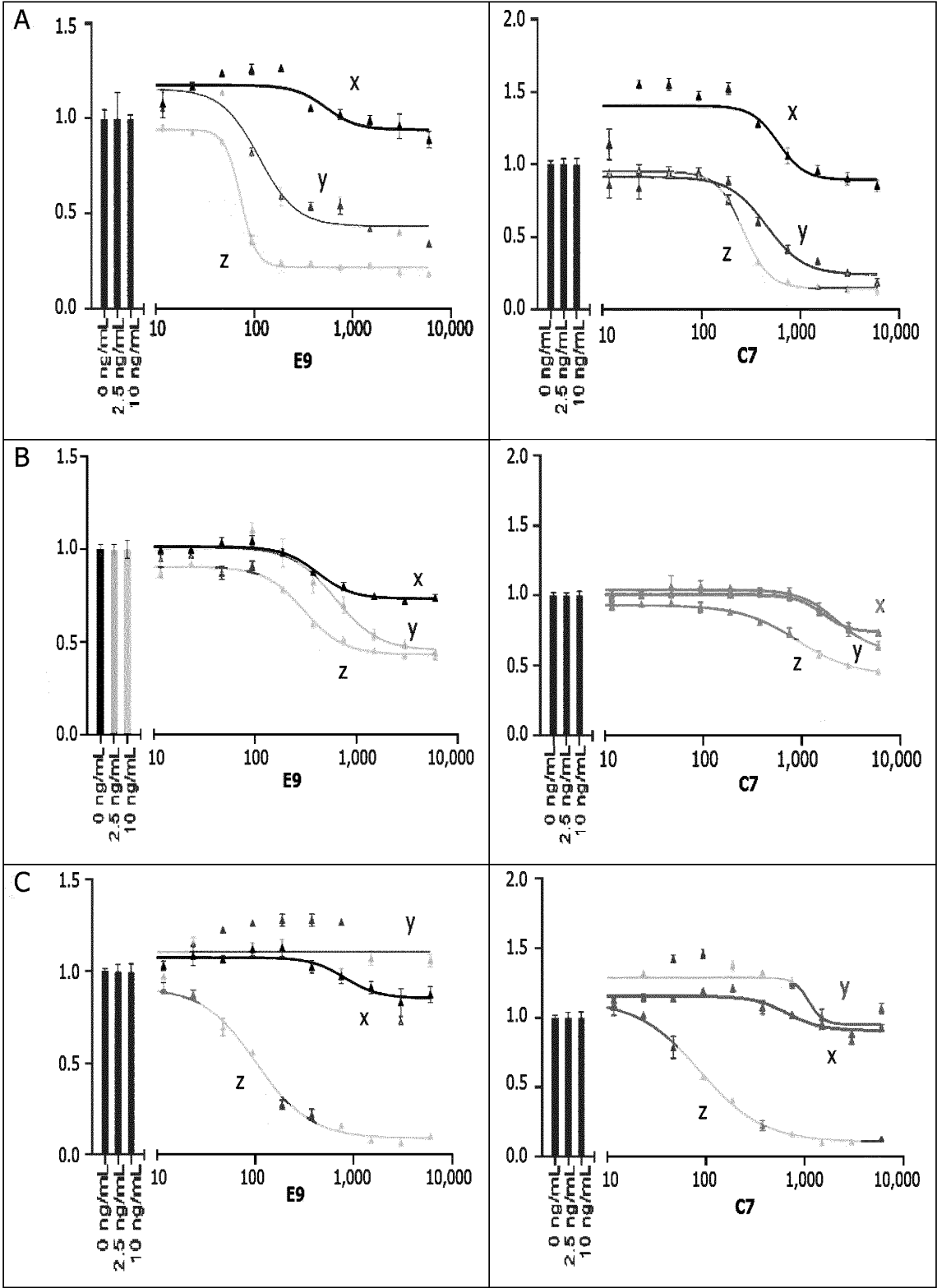


FIGURE 27

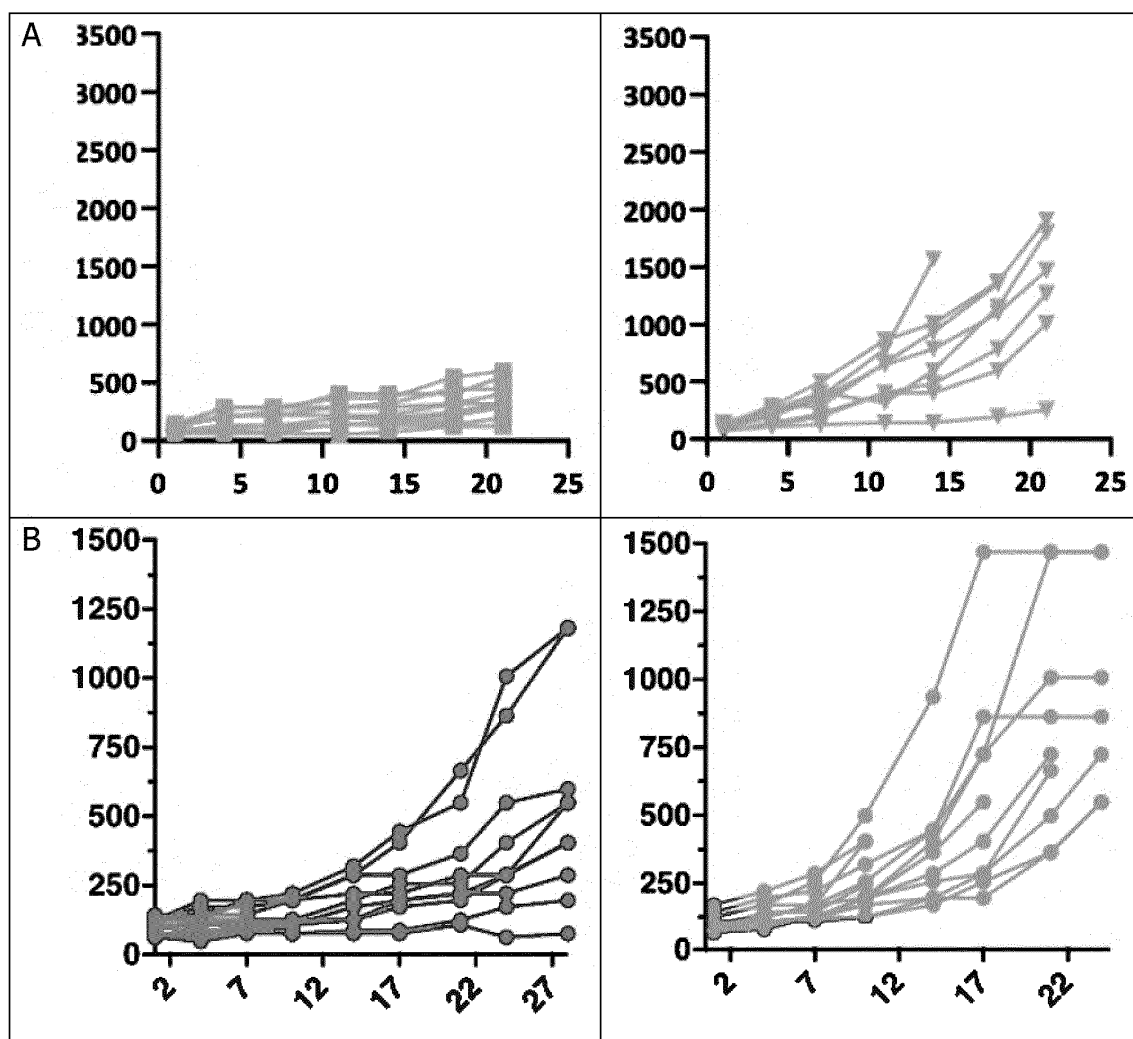


FIGURE 28

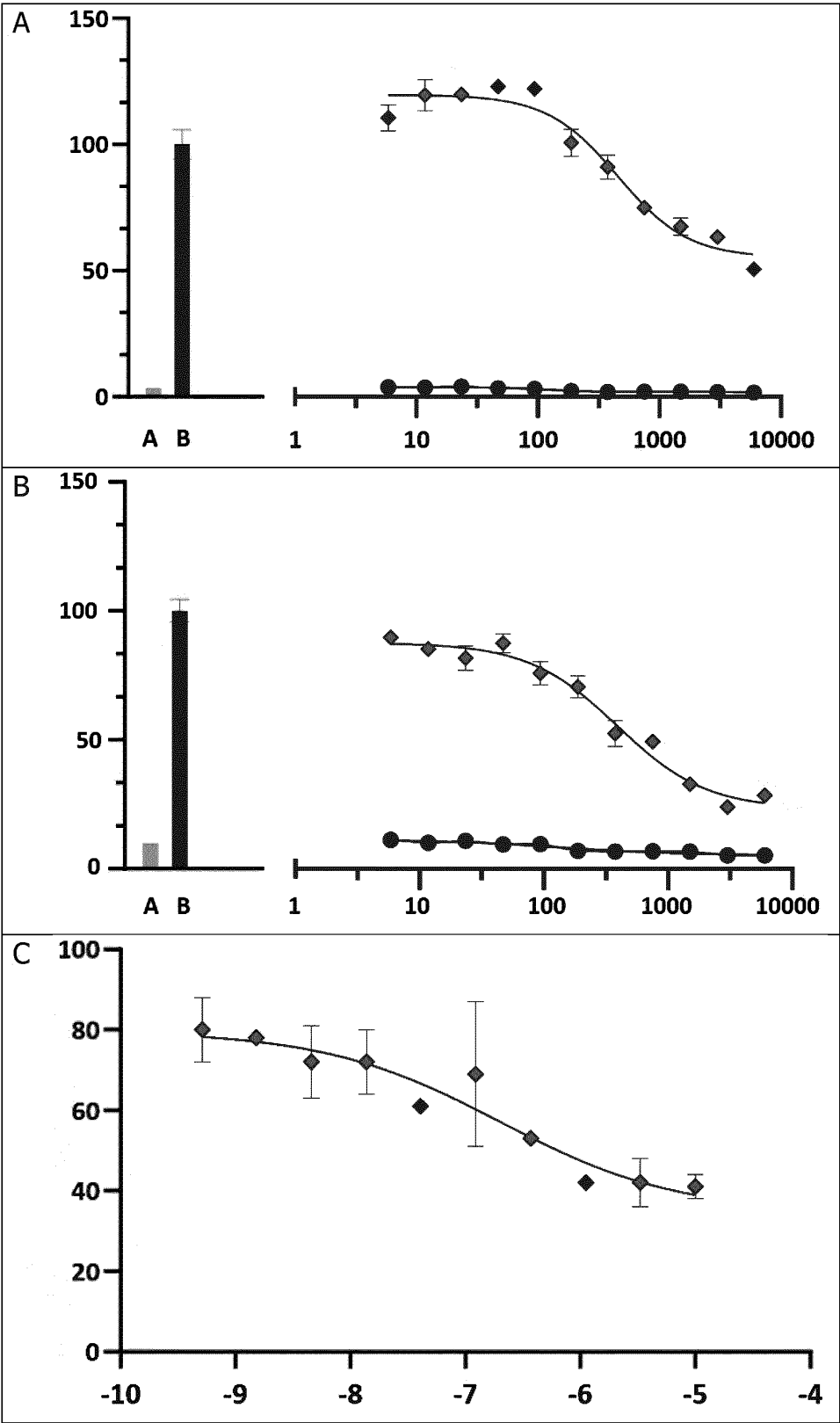


FIGURE 29

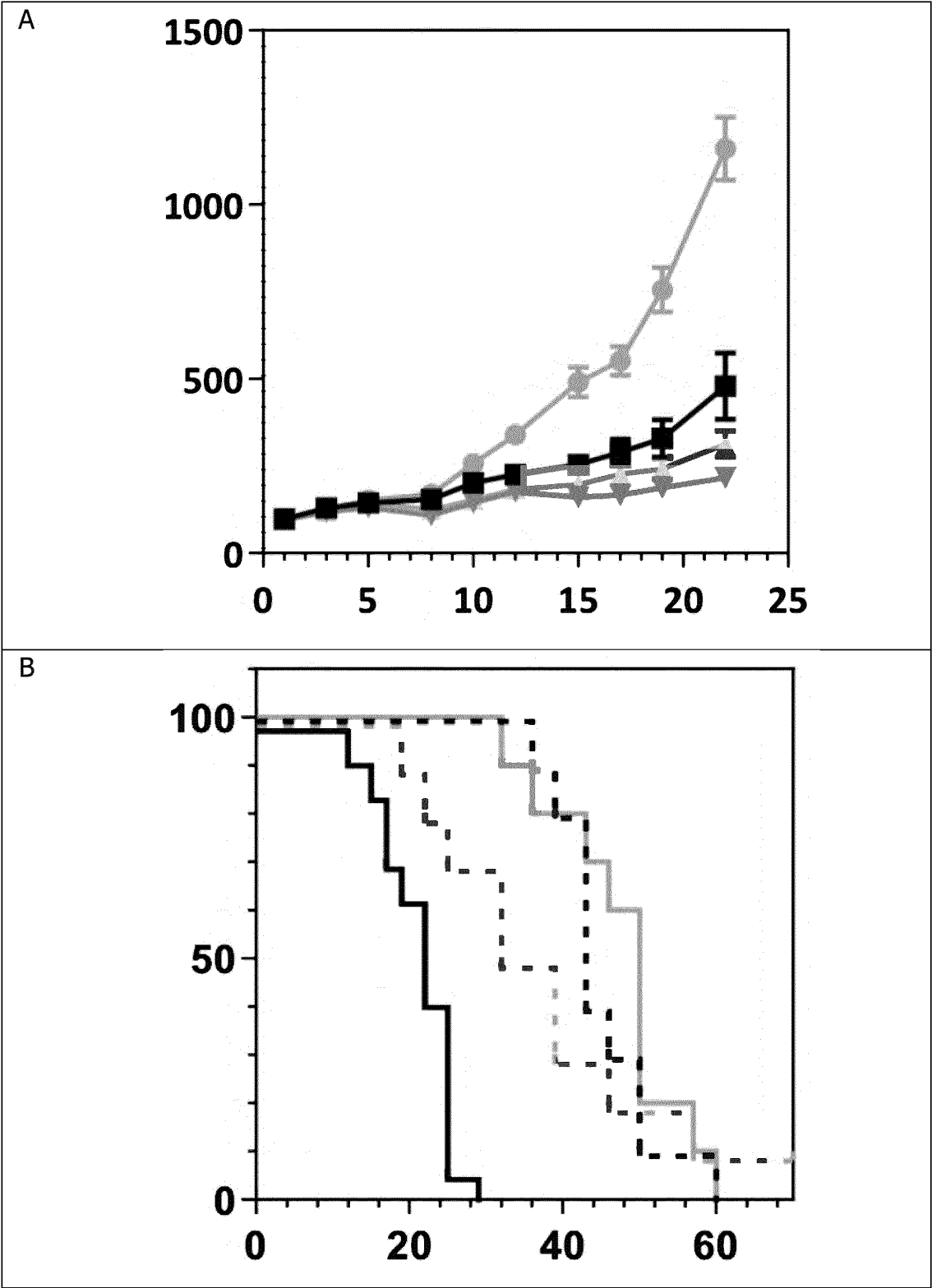


FIGURE 29 (cont)

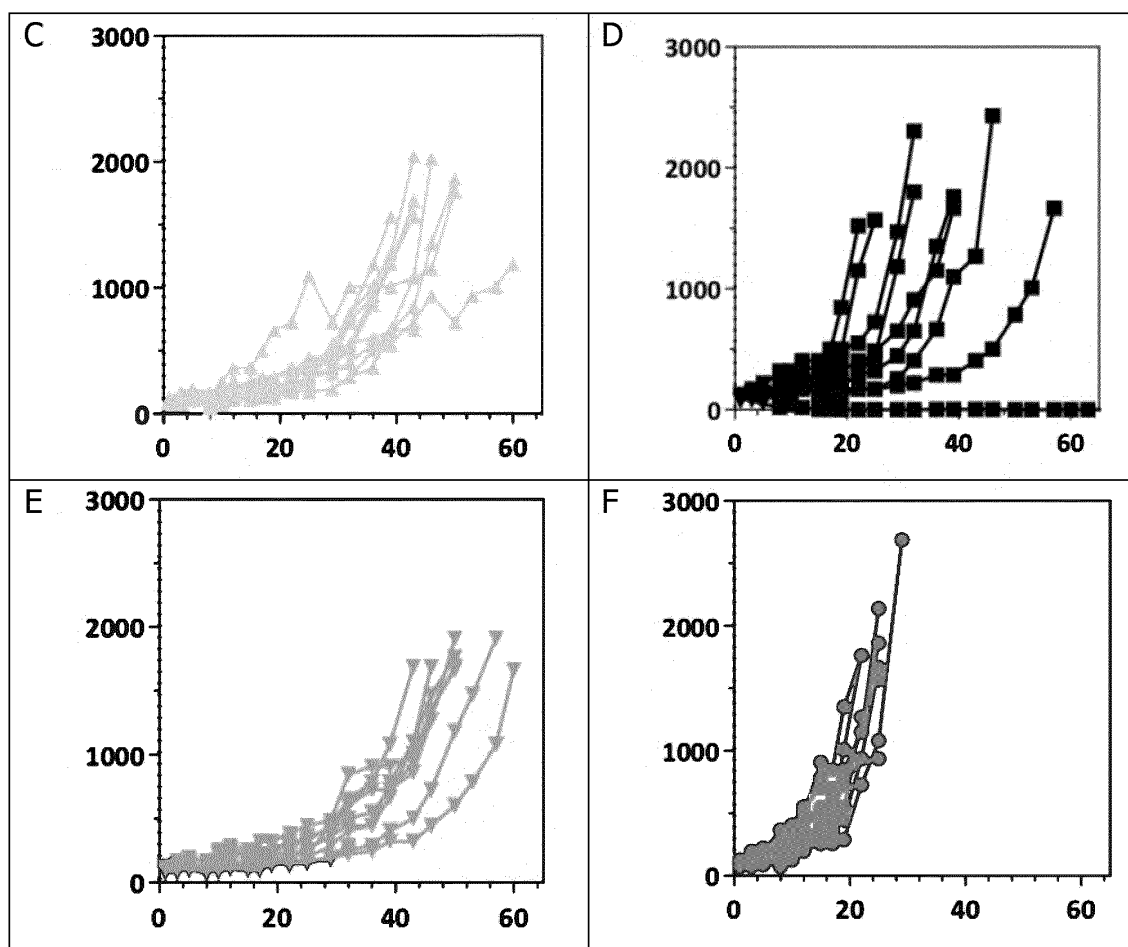


FIGURE 30

