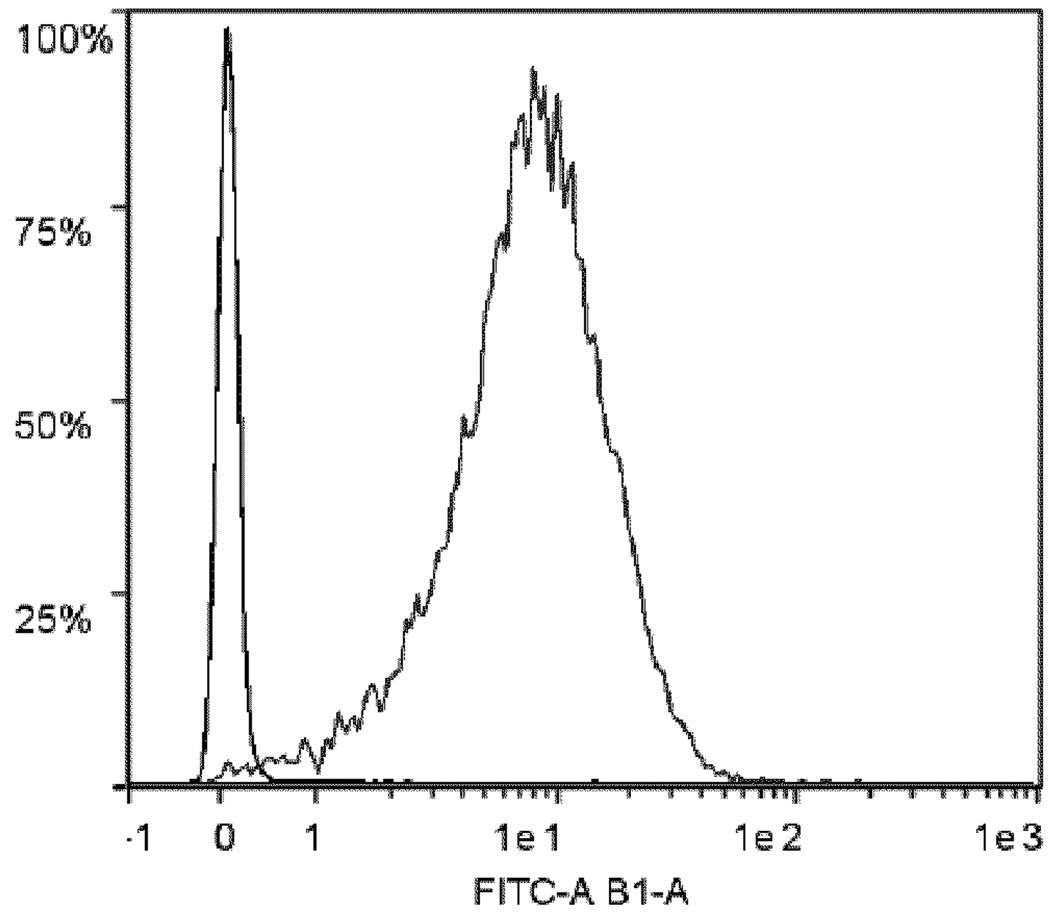
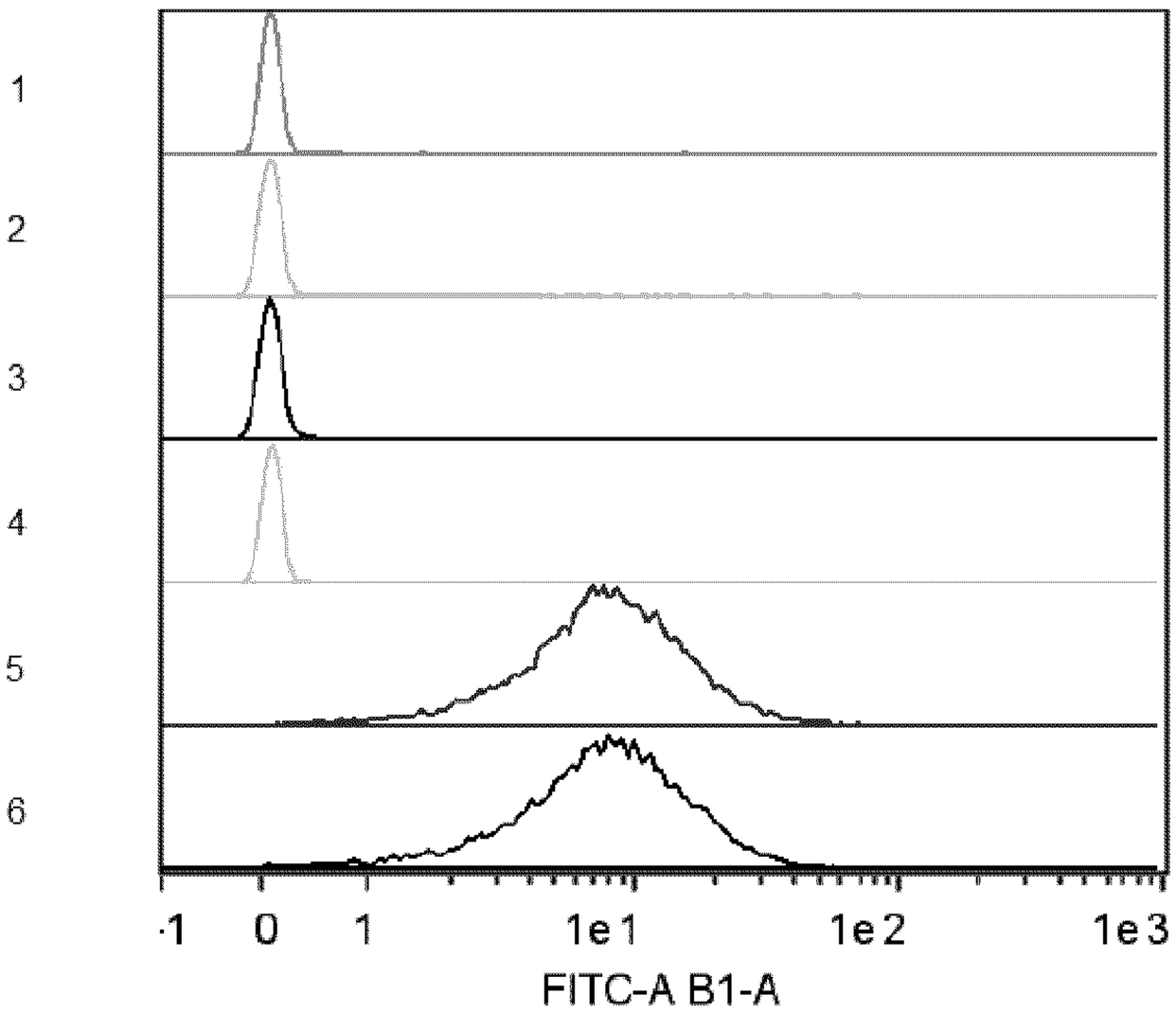


Color	Population	% Parent
	HER 3 positive [HEK293 O/E H3: 10D1]	98.98
	HER 3 positive [WT HEK293: 10D1]	0.60

Figure 1A



	Color	Population	% Parent
1		HER3 positive [WT HEK293: Isotype]	0.07
2		HER3 positive [WT HEK293: LJM716]	1.91
3		HER3 positive [WT HEK293: 10D1]	0.60
4		HER3 positive [HEK293 O/E H3: Isotyppe]	0.12
5		HER3 positive [HEK293 O/E H3: LJM716]	99.46
6		HER3 positive [HEK293 O/E H3: 10D1]	98.98

Figure 1B

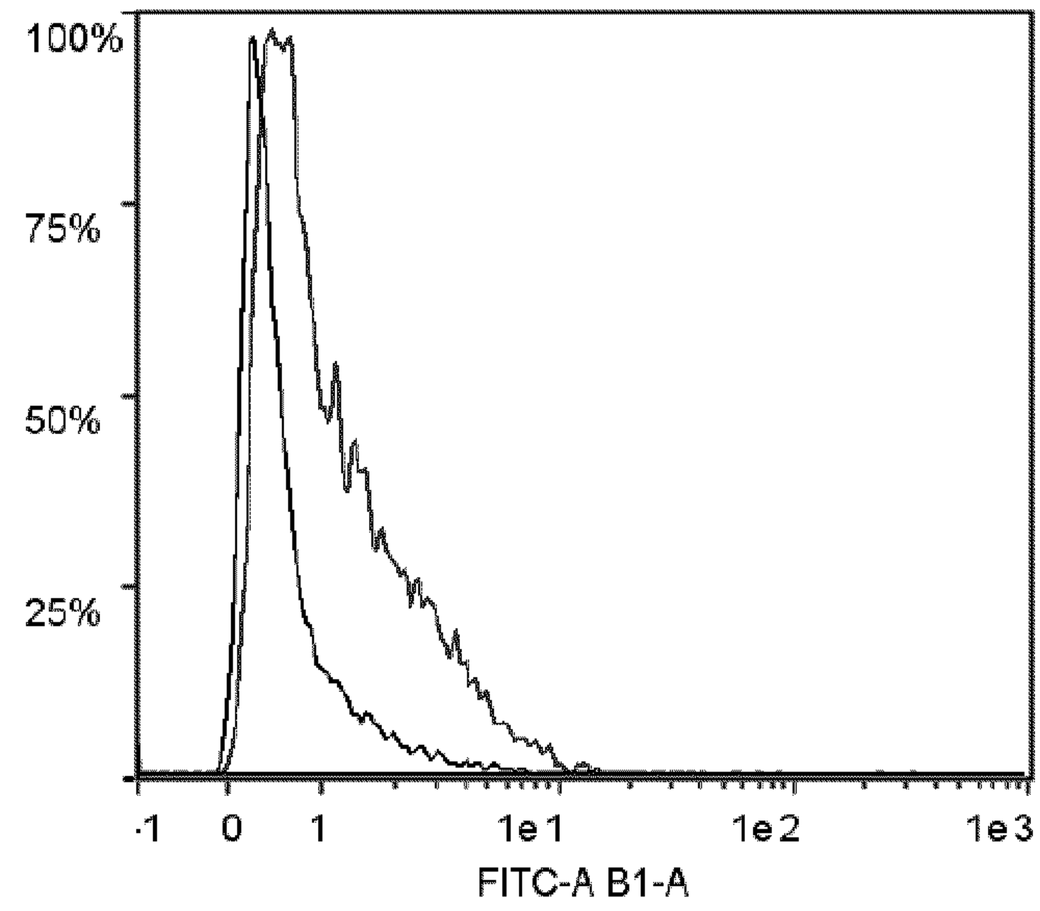


Figure 2A

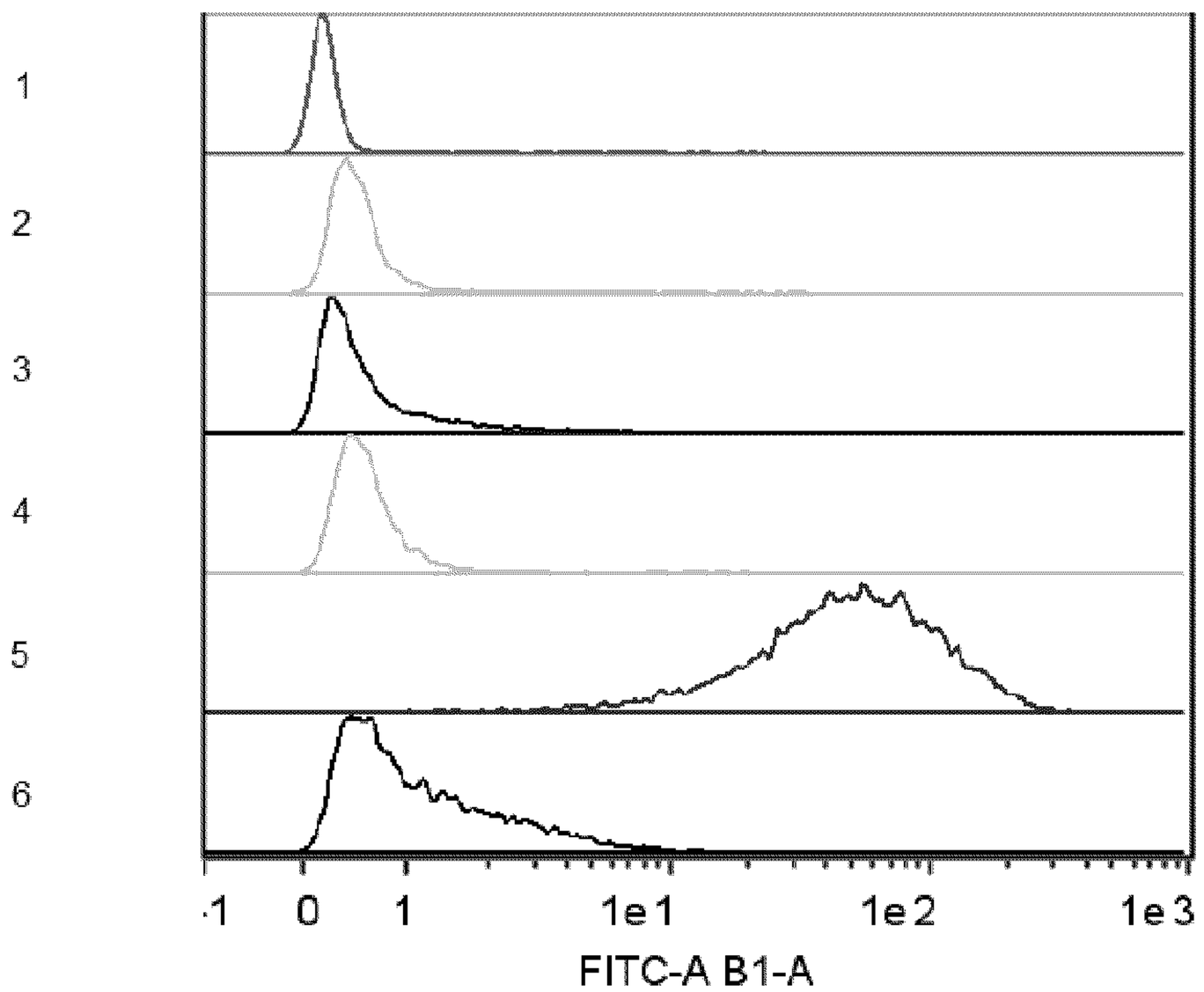


Figure 2B

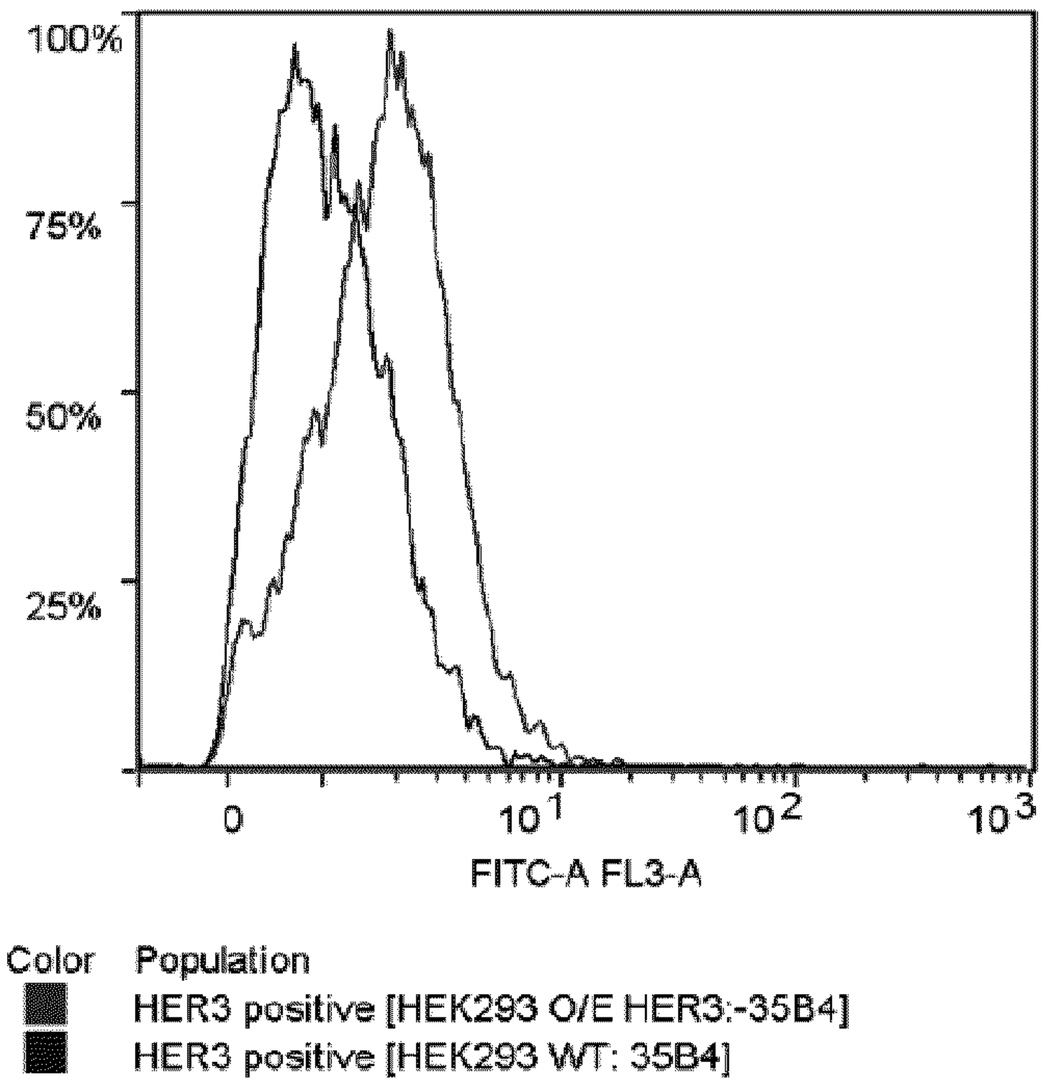


Figure 3A

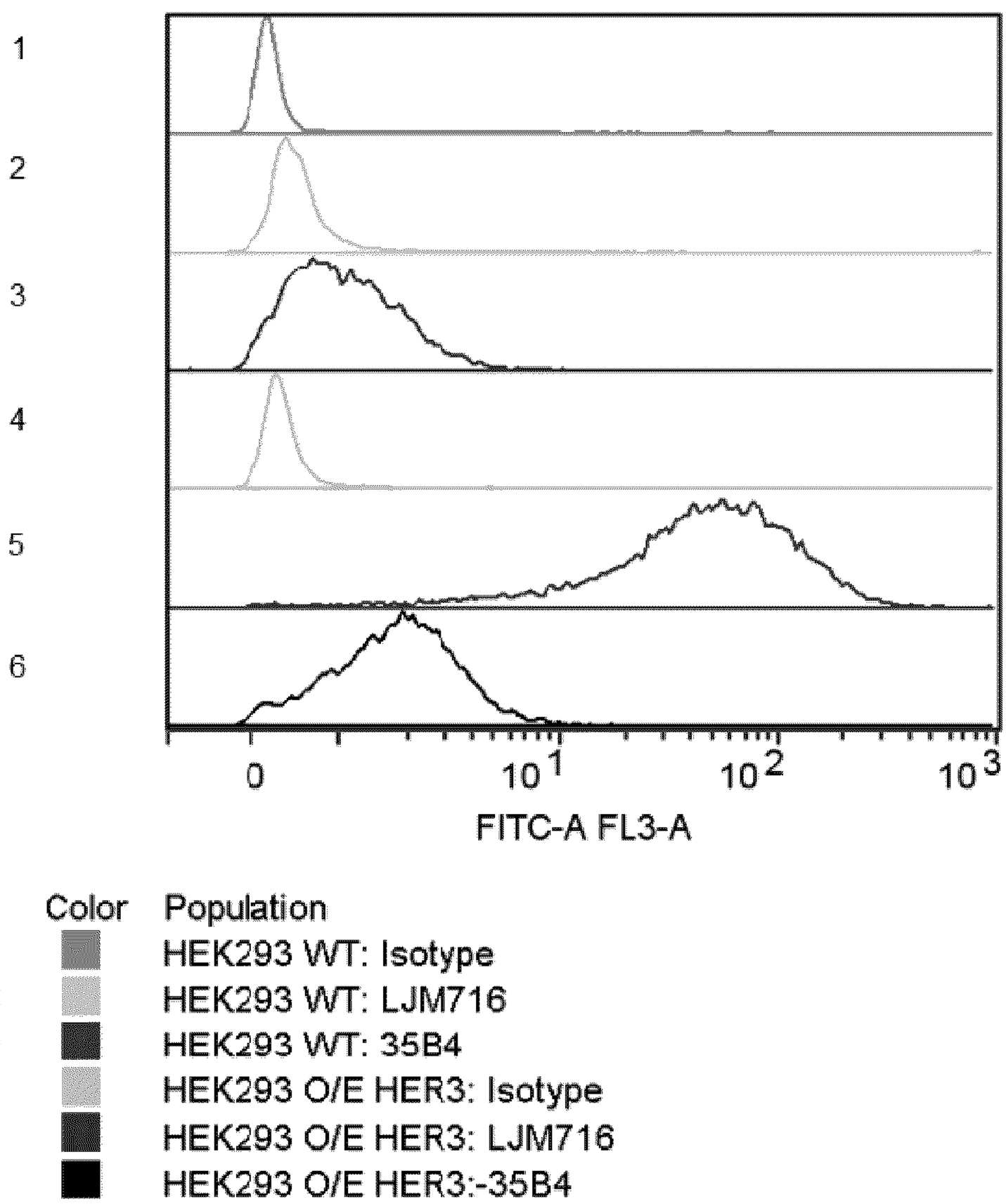


Figure 3B

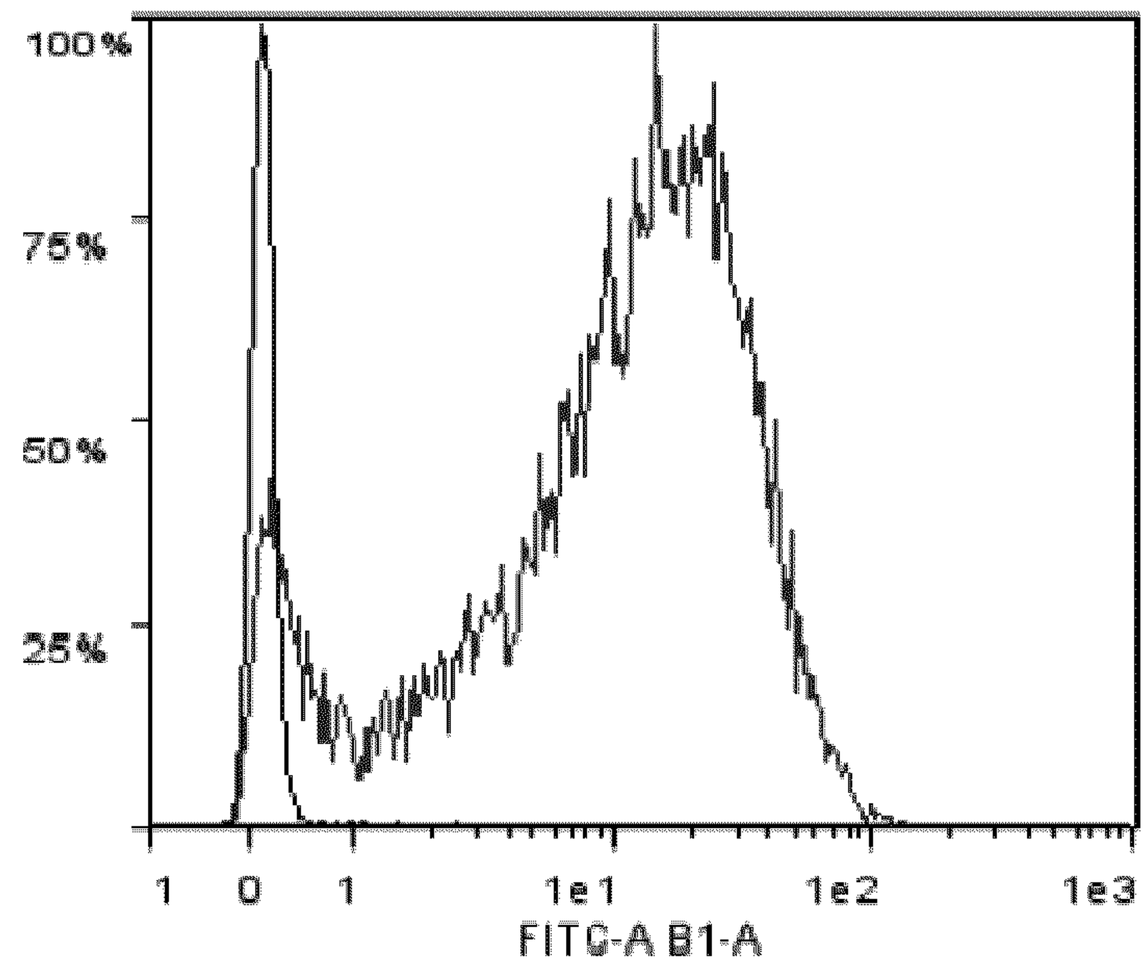
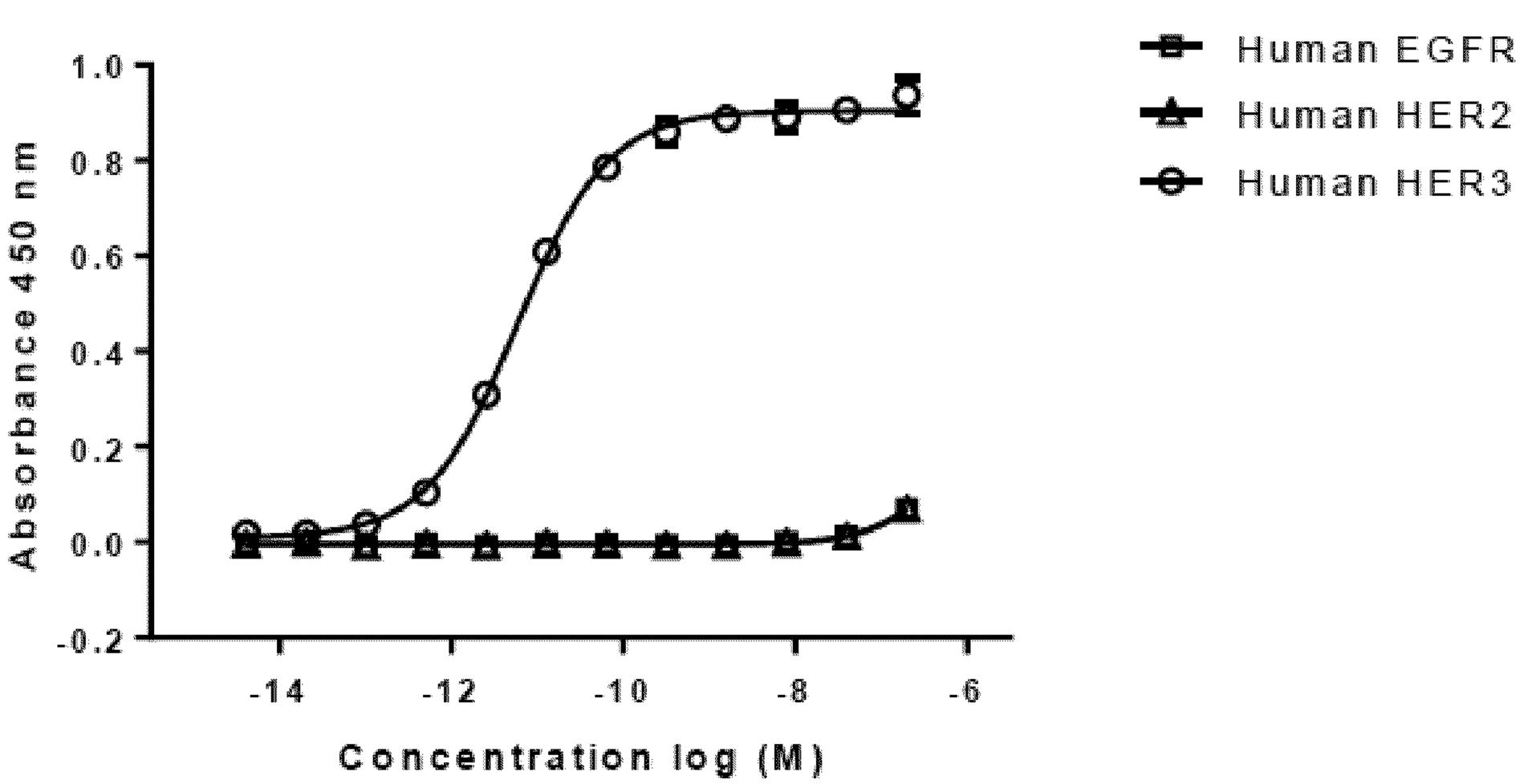
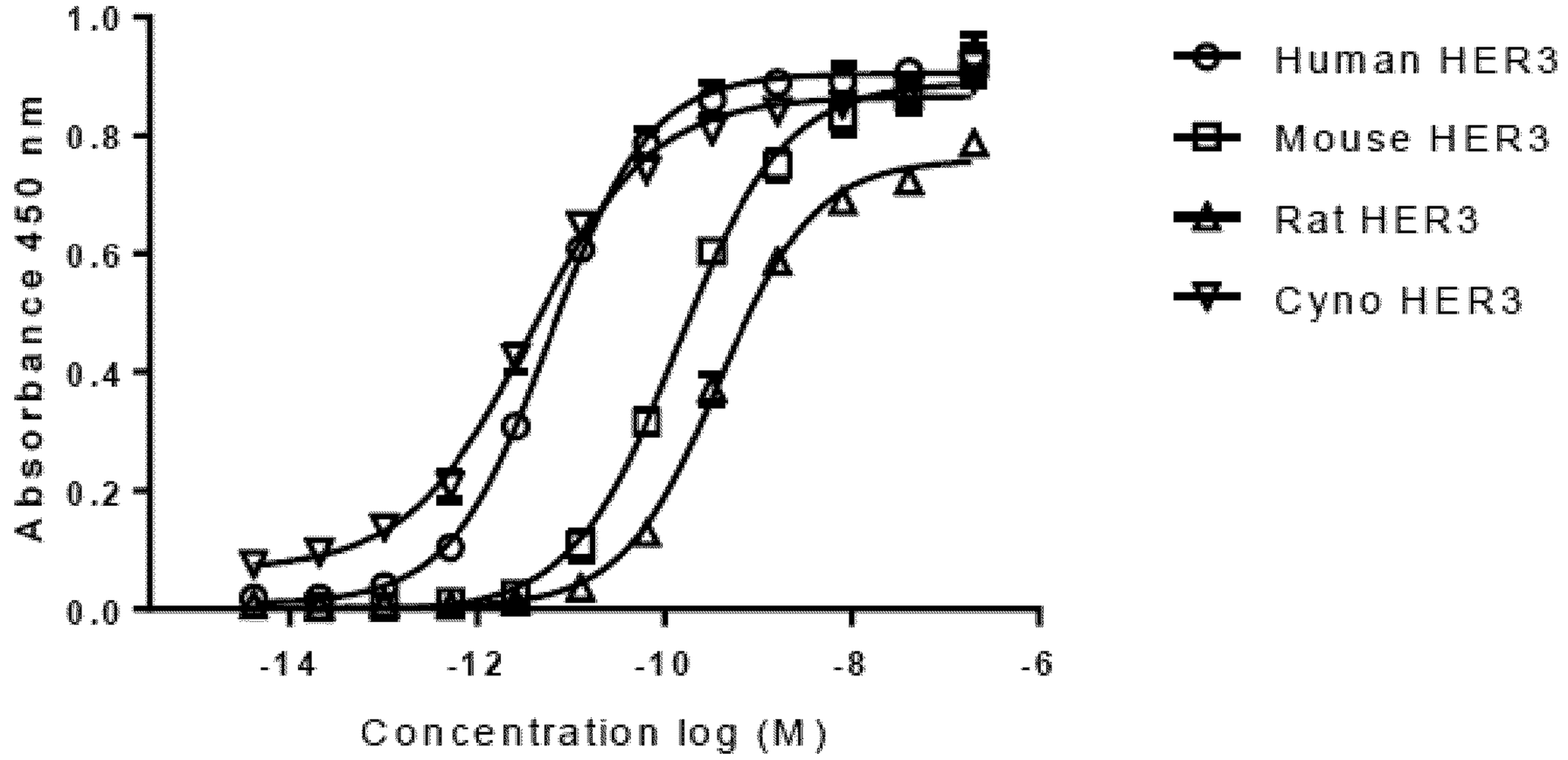


Figure 4



	Human EGFR	Human HER2	Human HER3
EC_{50} (M)	NA	NA	5.88E-12

Figure 5A



	Human HER3	Mouse HER3	Rat HER3	Cyno HER3
EC_{50} (M)	5.88E-12	1.37E-10	3.72E-10	3.68E-12

Figure 5B

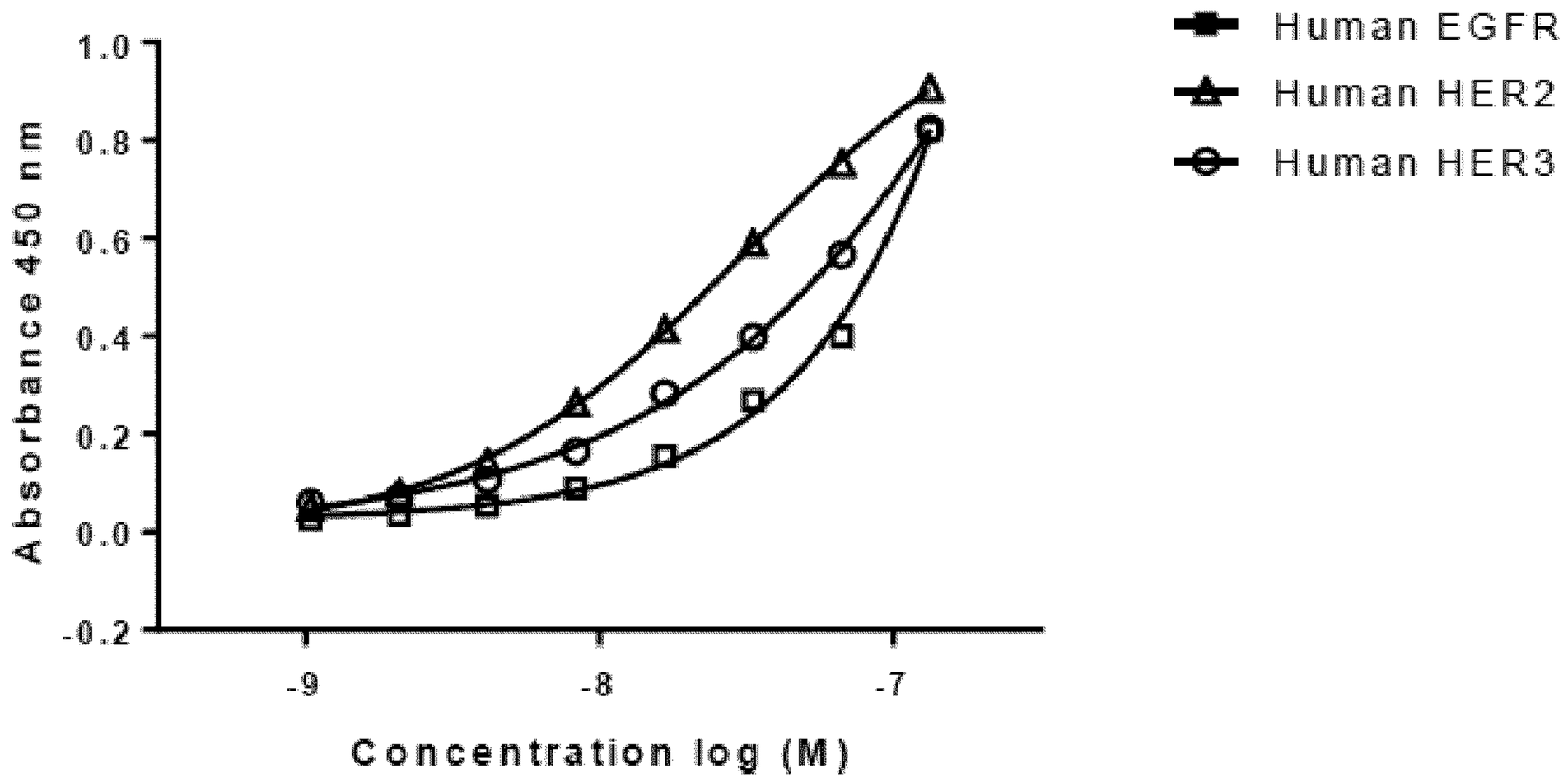


Figure 6A

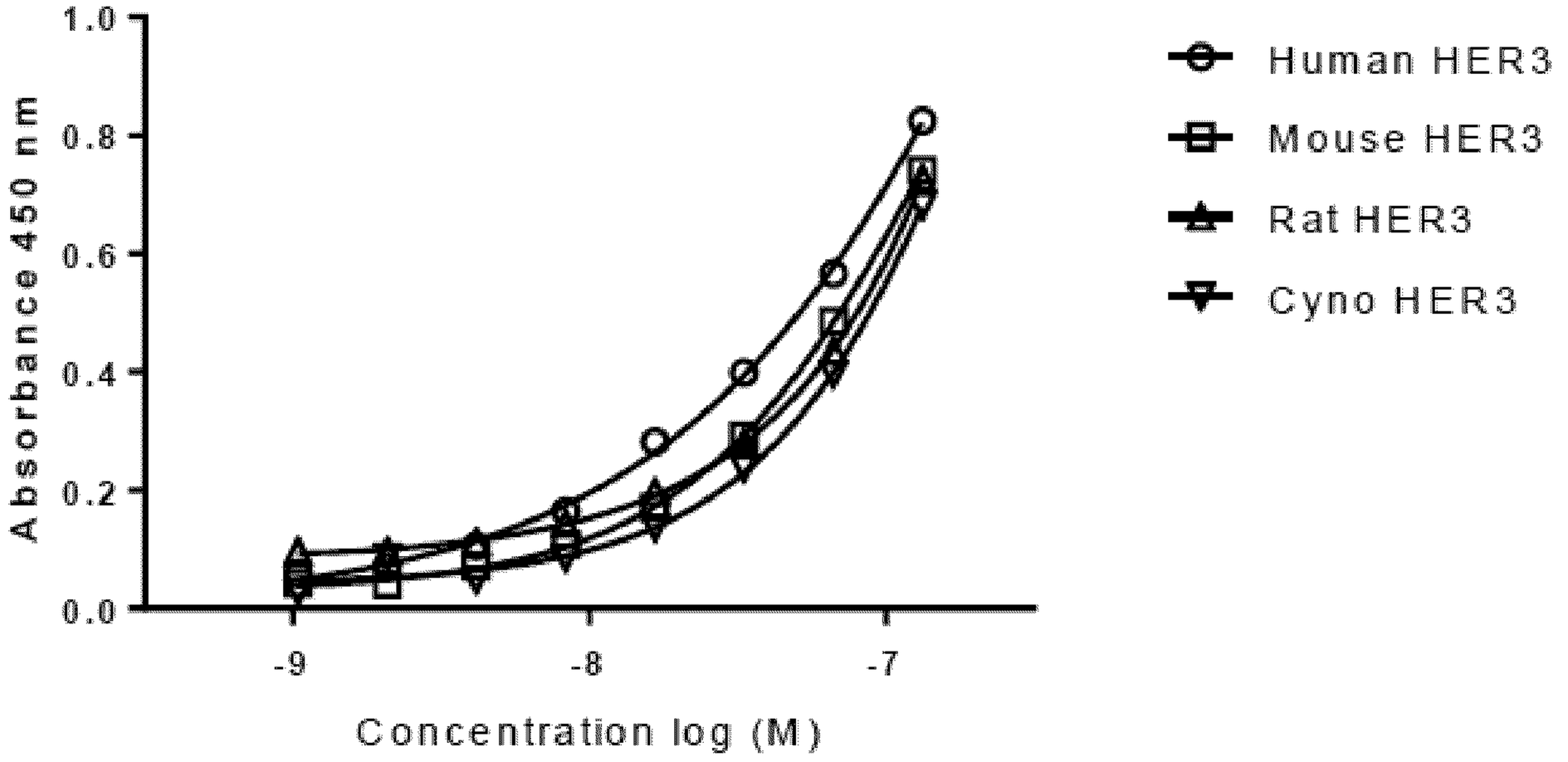


Figure 6B

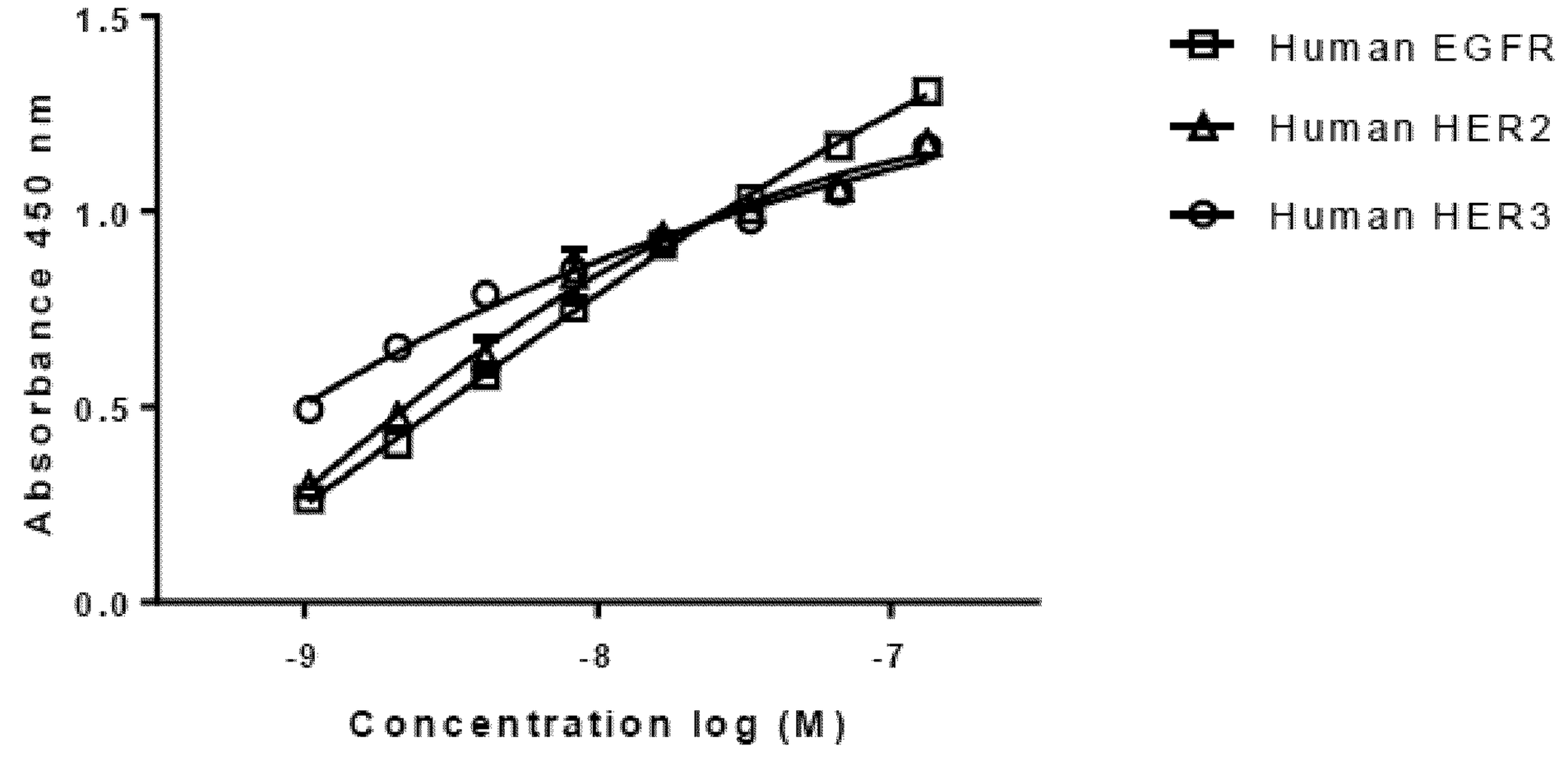


Figure 7A

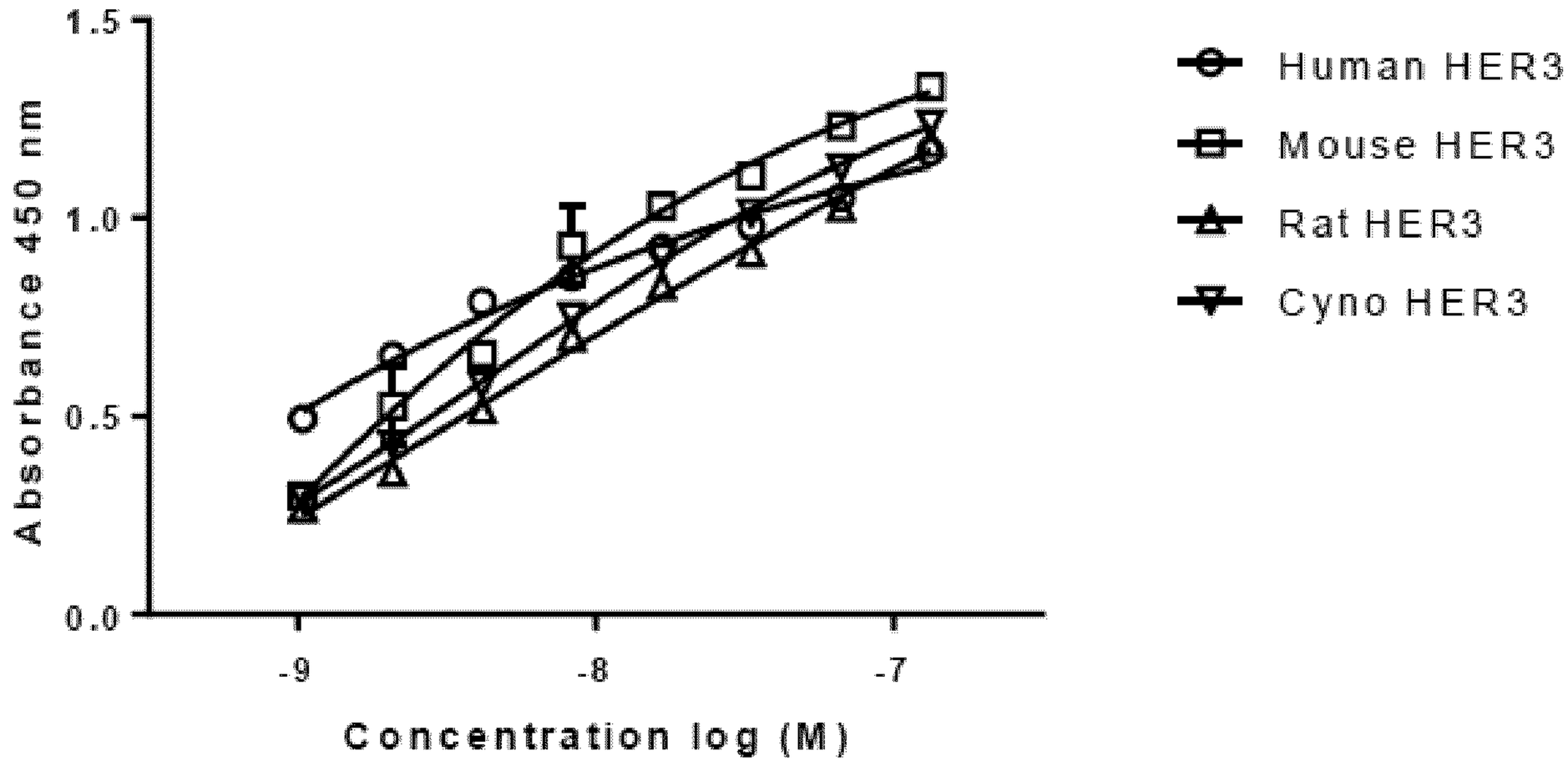
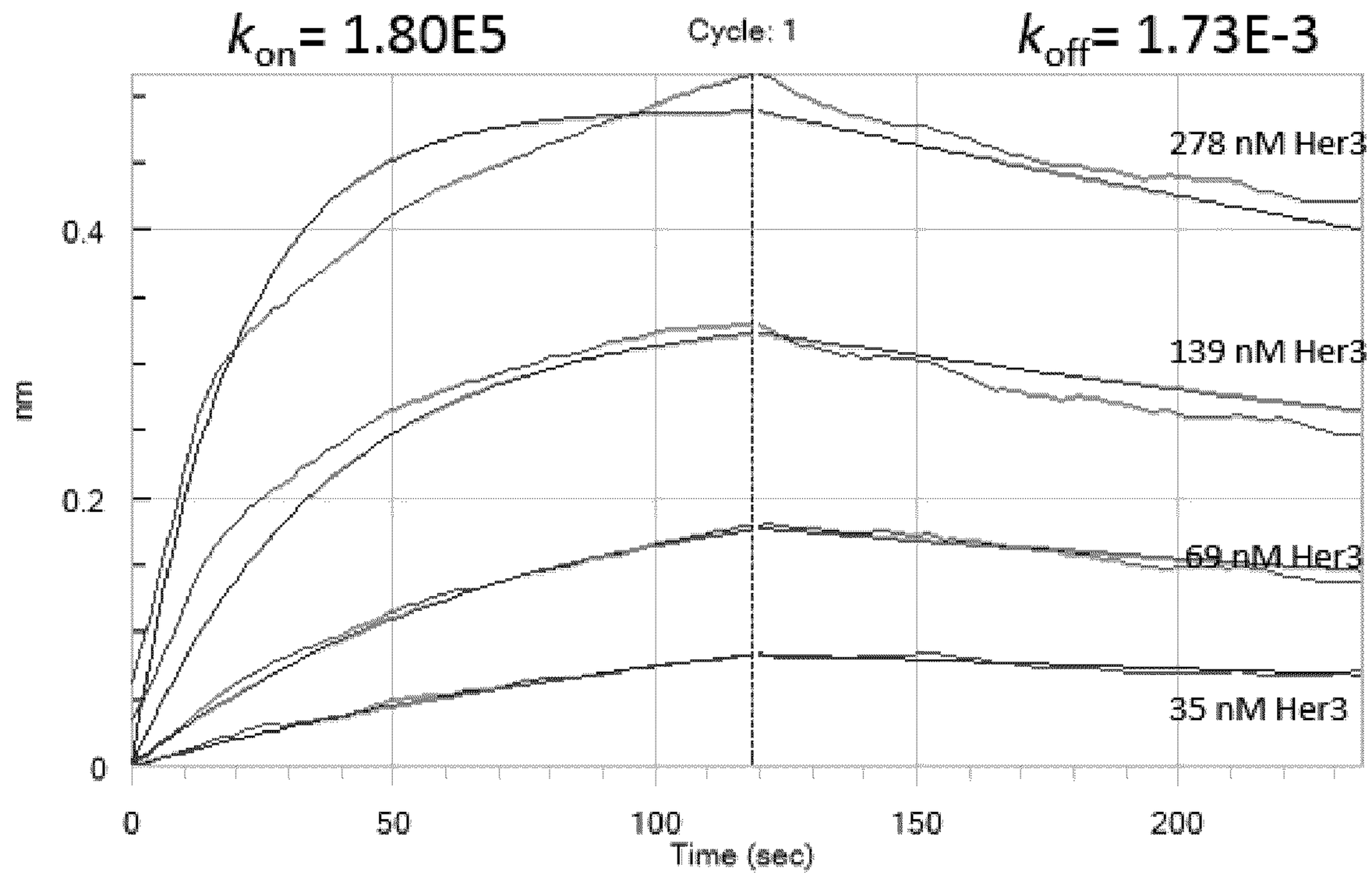

1.5
1.0
0.5
0.0
Absorbance 450 nm
-9
-8
-7
Concentration log (M)
Human HER3
Mouse HER3
Rat HER3
Cyno HER3

Figure 7B



k_d= 9.58 nM

R^2 = 0.9898

Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
10D1p	1	278	0.5079	9.58E-09	9.70E-10	1.80E+05	8.22E+03	1.73E-03	1.56E-04	0.5055	0.0063	5.18E-02	0.4886	96.7	0.0301	0.9898
10D1p	1	35	0.0794	9.58E-09	9.70E-10	1.80E+05	8.22E+03	1.73E-03	1.56E-04	0.1718	0.01	8.03E-03	0.1348	78.5	0.0301	0.9898
10D1p	1	139	0.3278	9.58E-09	9.70E-10	1.80E+05	8.22E+03	1.73E-03	1.56E-04	0.359	0.0076	2.68E-02	0.3359	93.5	0.0301	0.9898
10D1p	1	69	0.1744	9.58E-09	9.70E-10	1.80E+05	8.22E+03	1.73E-03	1.56E-04	0.2471	0.0089	1.42E-02	0.2169	87.8	0.0301	0.9898

Figure 8

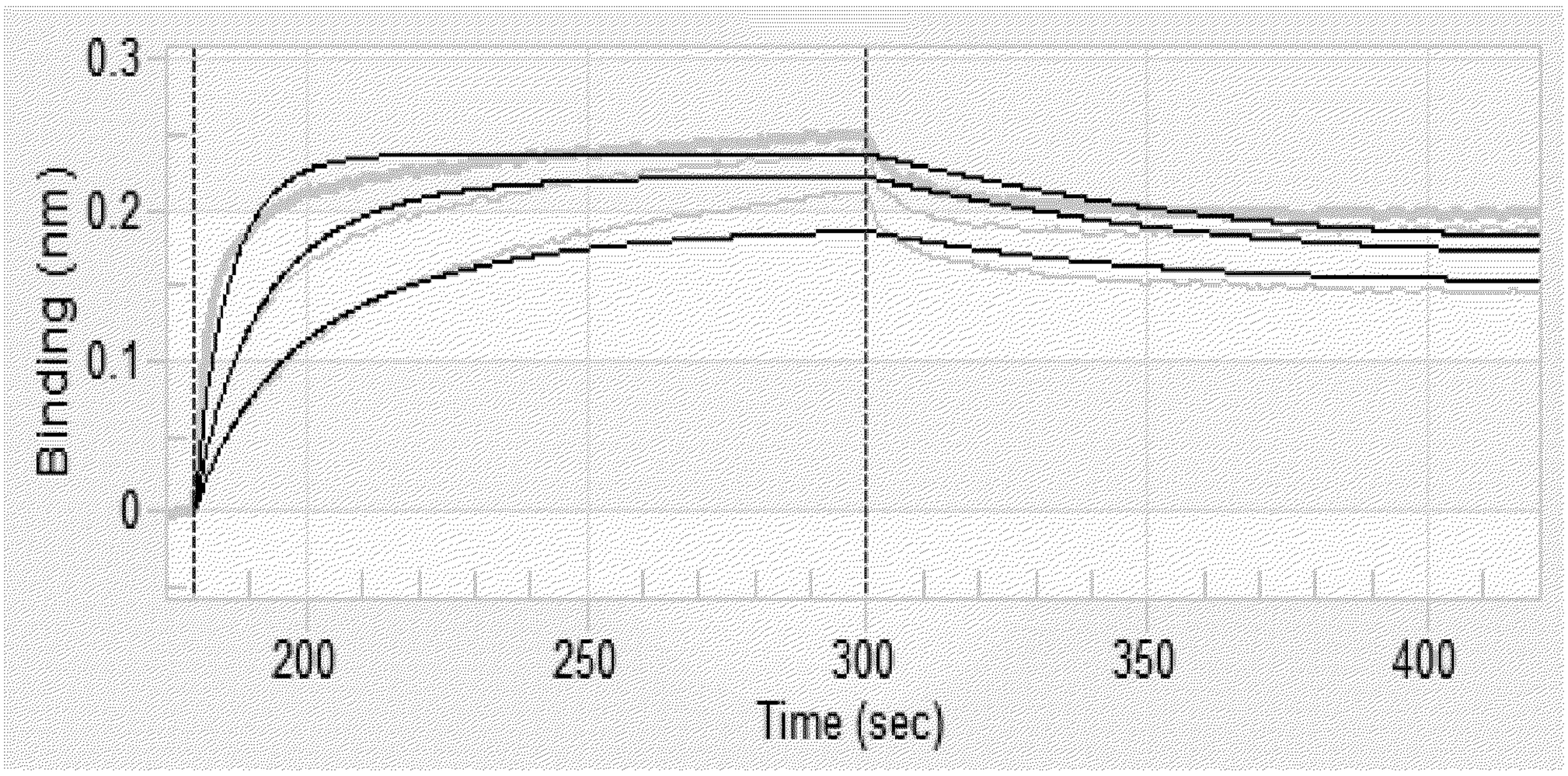


Figure 9

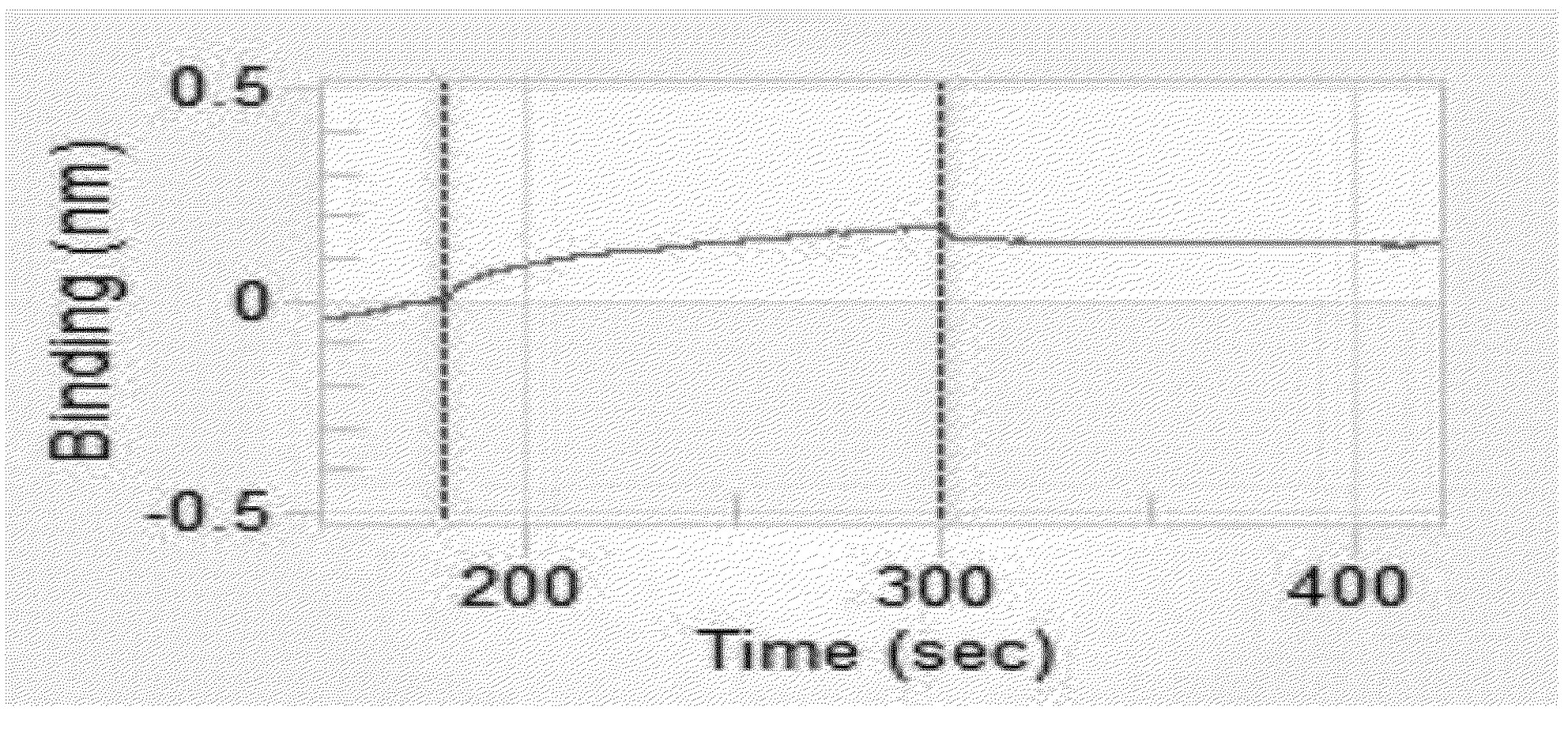


Figure 10

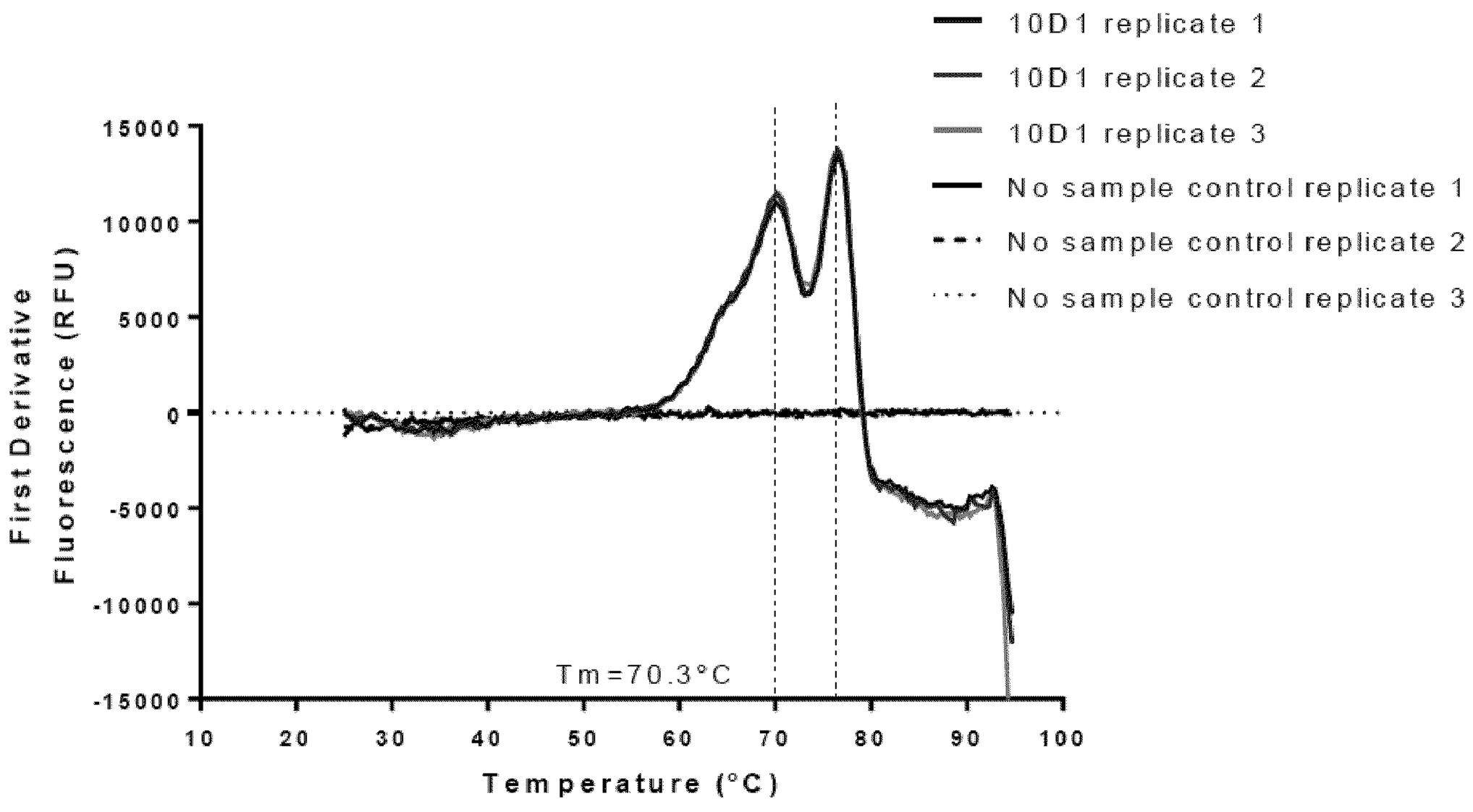


Figure 11

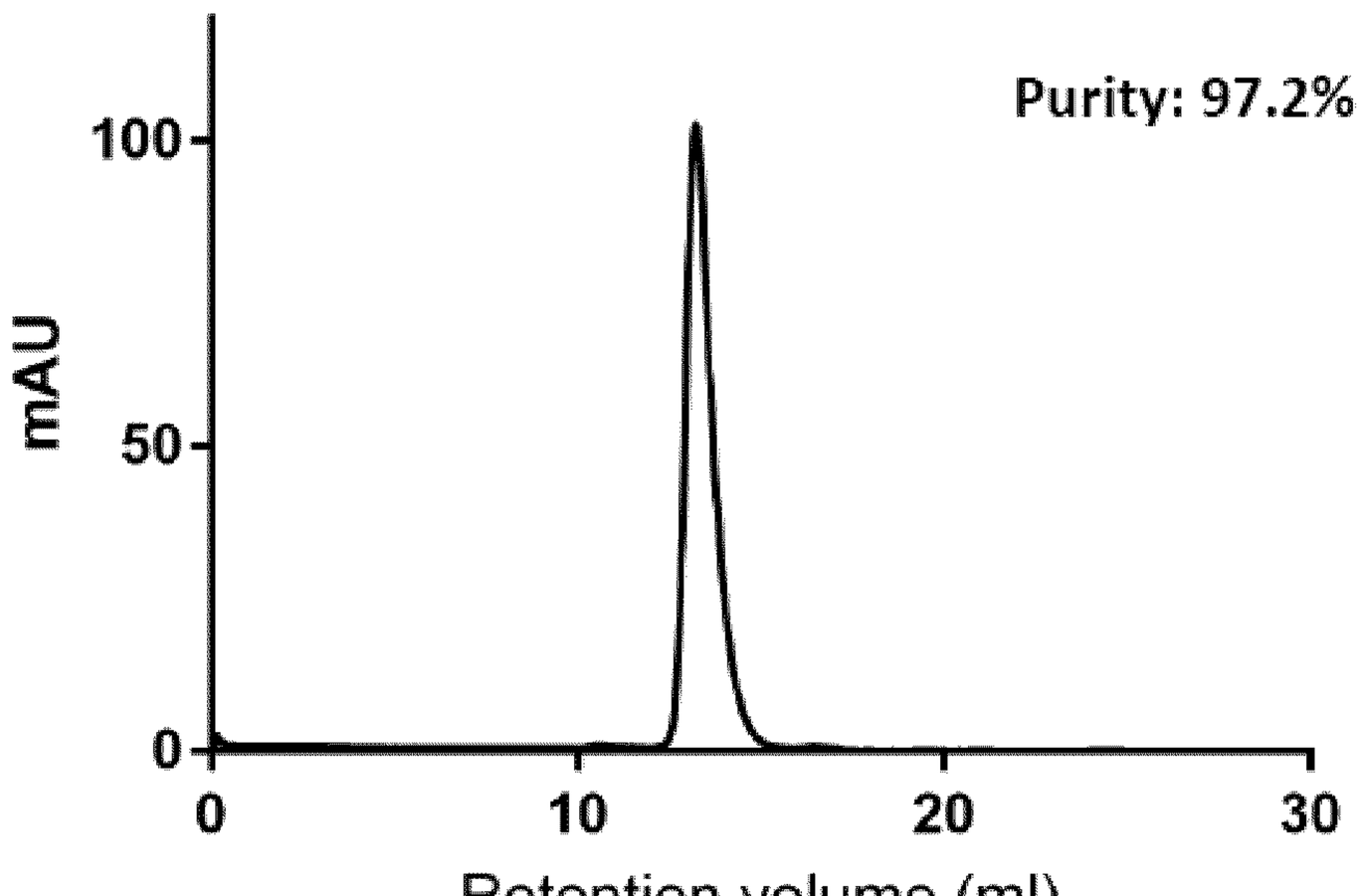


Figure 12

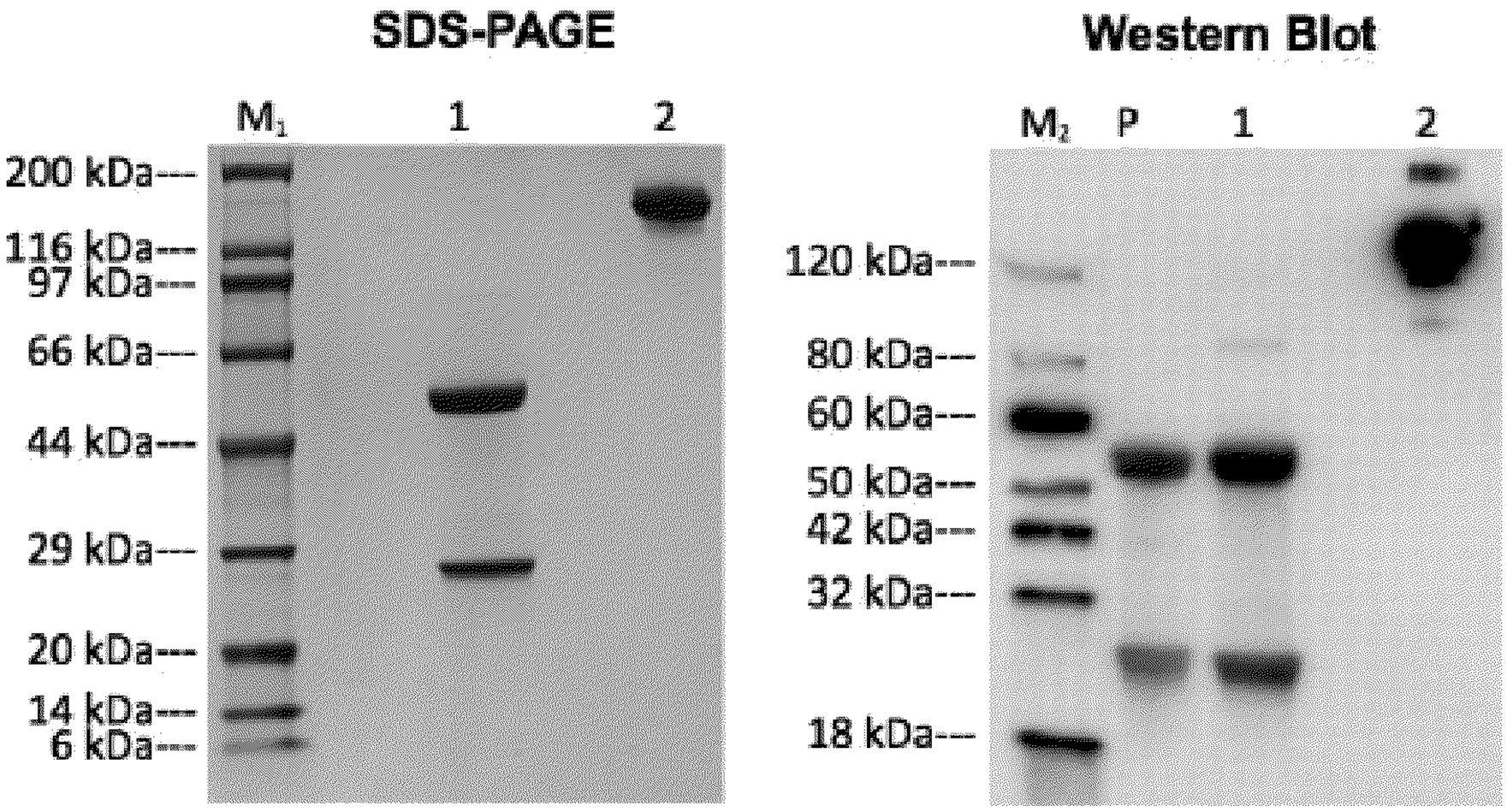

SDS-PAGE
M1
1
2
200 kDa
116 kDa
97 kDa
66 kDa
44 kDa
29 kDa
20 kDa
14 kDa
6 kDa
Western Blot
M2
P
1
2
120 kDa
80 kDa
60 kDa
50 kDa
42 kDa
32 kDa
18 kDa

Figure 13

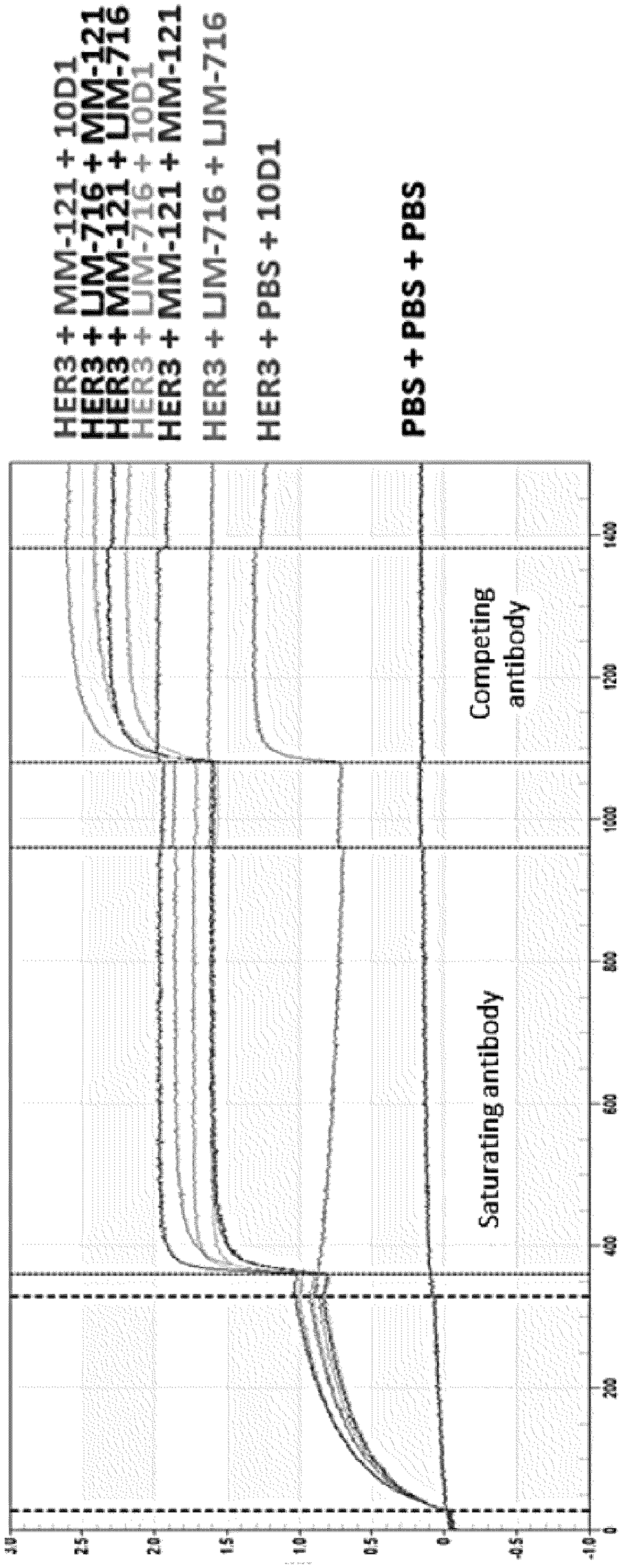

MM-121 + 10D1
UM-716 + MM-121
MM-121 + UM-716
UM-716 + 10D1
MM-121 + MM-121
UM-716 + UM-716
PBS + 10D1
PBS + PBS
HER3 +++
HER3 +++
HER3 ++
HER3 +
HER3 +
HER3 +
Competing antibody
Saturating antibody
1400
1200
1000
800
600
400
200
0
-10
-5
0
5
10
15
20
25
30
X-Axis: Time (s)
Y-Axis: Shift (nm)

Figure 14A

		Competing Antibody		
		10D1	MM-121	UM-716
Saturating Antibody	10D1	x	x	x
	MM-121	0.757	x	0.729
	UM-716	0.638	0.693	x

Figure 14B

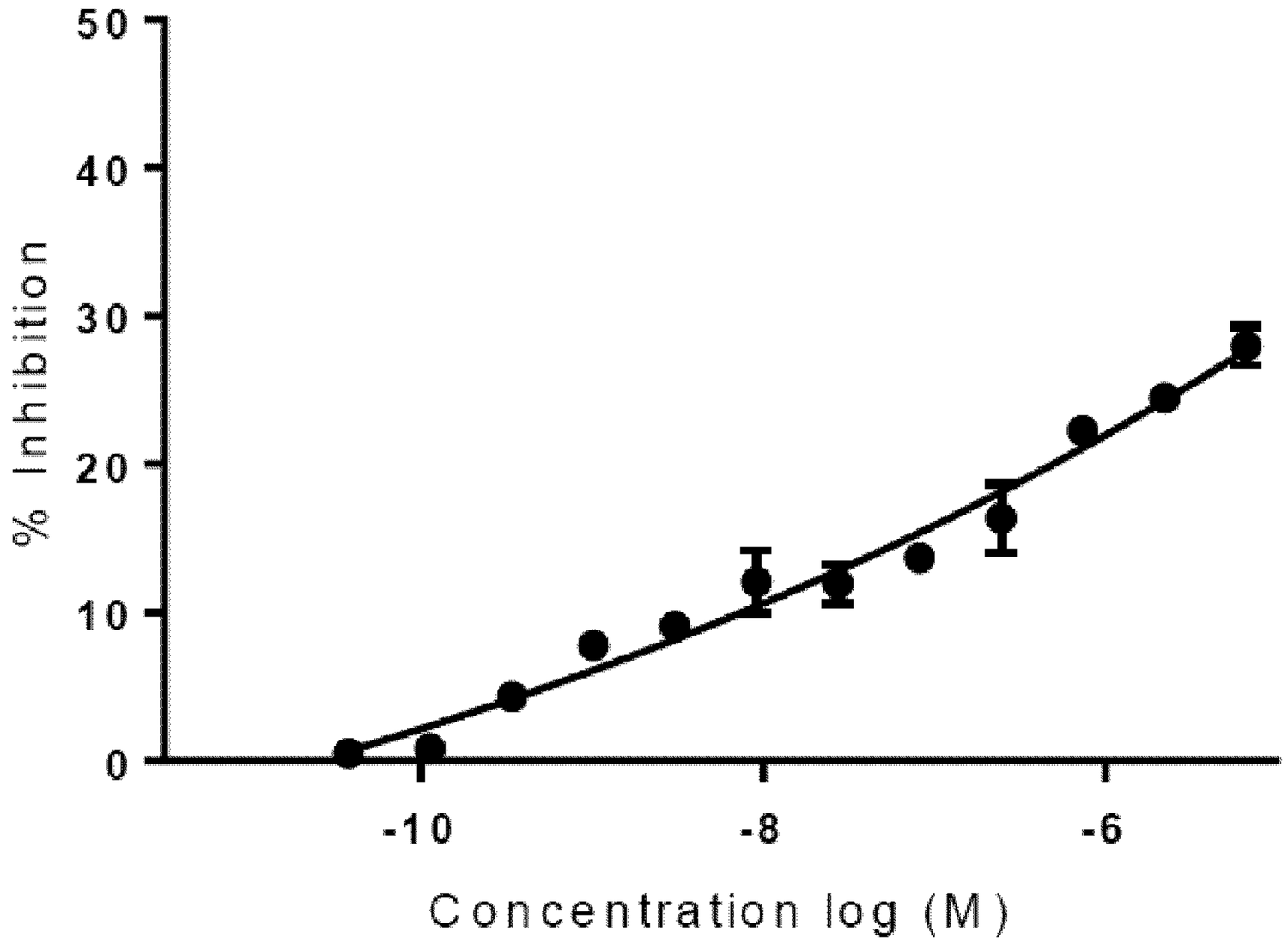


Figure 15

Solid Tumor	Cell Line	mRNA Expression (Data from CCLE*)						Protein expression (Data based on FACS**)		
		EGFR	HER2	HER3	HER4	EGF	NRG1	EGFR	HER2	HER3
Gastric	N87	7.08	13.18	9.67	3.83	4.08	4.22	358	618	5.6
	SNU16	6.88	7.8	11.06	4.04	3.78	4.26	13.6	28.3	1.87
Colorectal	HT29	6.54	8.11	10.8	3.81	3.83	4.53	27.5	20.3	4.2
Head and Neck	FaDu	7.99	7.36	8.35	4.01	3.89	4.96	65.1	11.6	1.5
Lung	A549	7.29	6.79	5.18	3.85	4.2	8.81	19	17.7	7.4
	HCC95	7.33	7.06	7.31	3.85	4.19	11.24	100.8	44.5	8.2
Ovarian	OvCAR8	6.19	6.72	8.24	3.86	4.72	6.65	44.5	130.5	4.7
Kidney	ACHN	7.81	6.78	6.32	3.8	4.66	8.04	93.6	67.5	4

*CCLE gene expression data is log2-transformed robust multi-array (RMA)-normalized data generated from Affymetrix gene chips. The expression values in rather are relative

** Median fluorescence intensity normalized to isotype calculated by FlowLogic.

Figure 16A

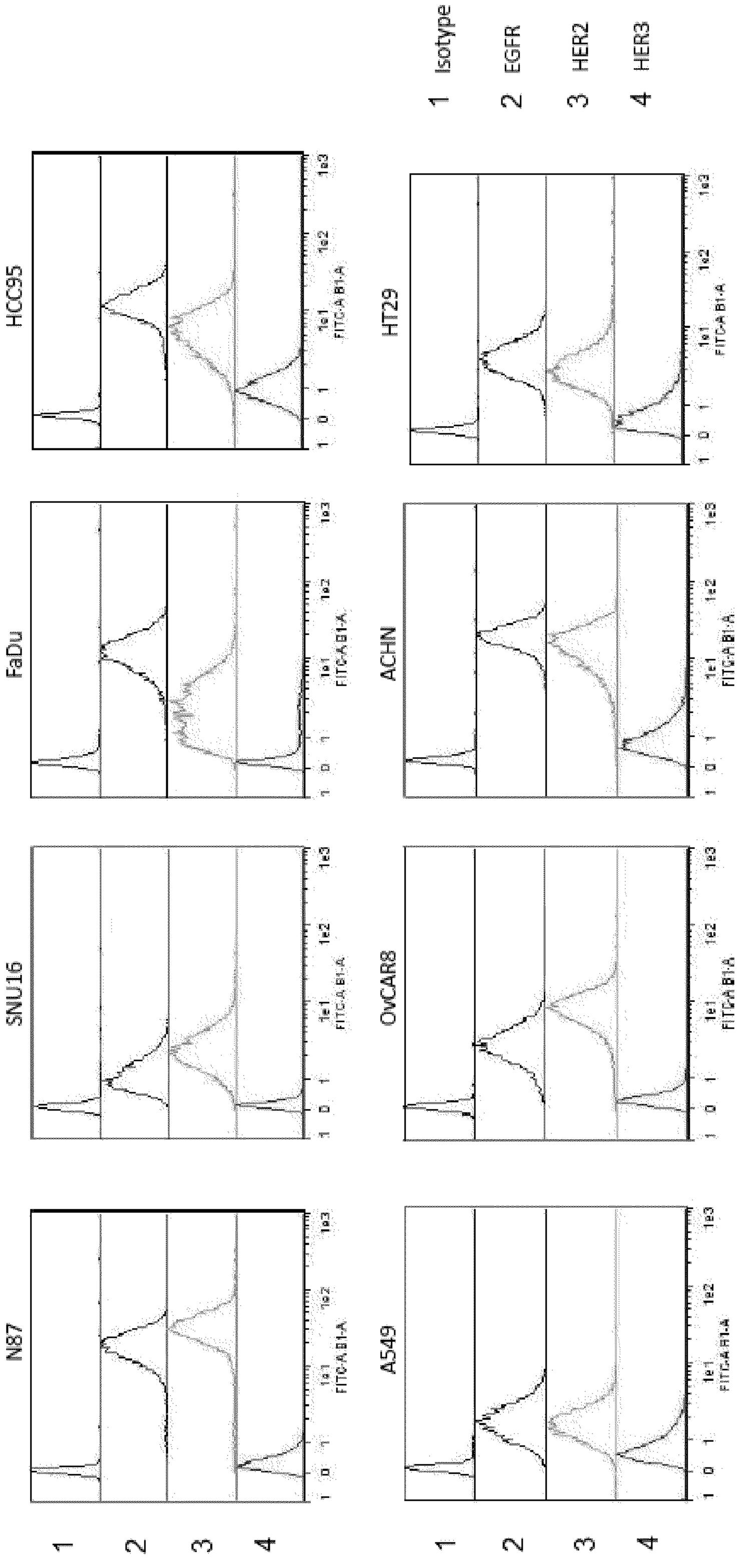

1 Isotype
2 EGFR
3 HER2
4 HER3
HCC95
HT29
FaDu
ACHN
SNU16
OvCAR8
N87
A549
FITC-A B1-A
1 2 3 4

Figure 16B

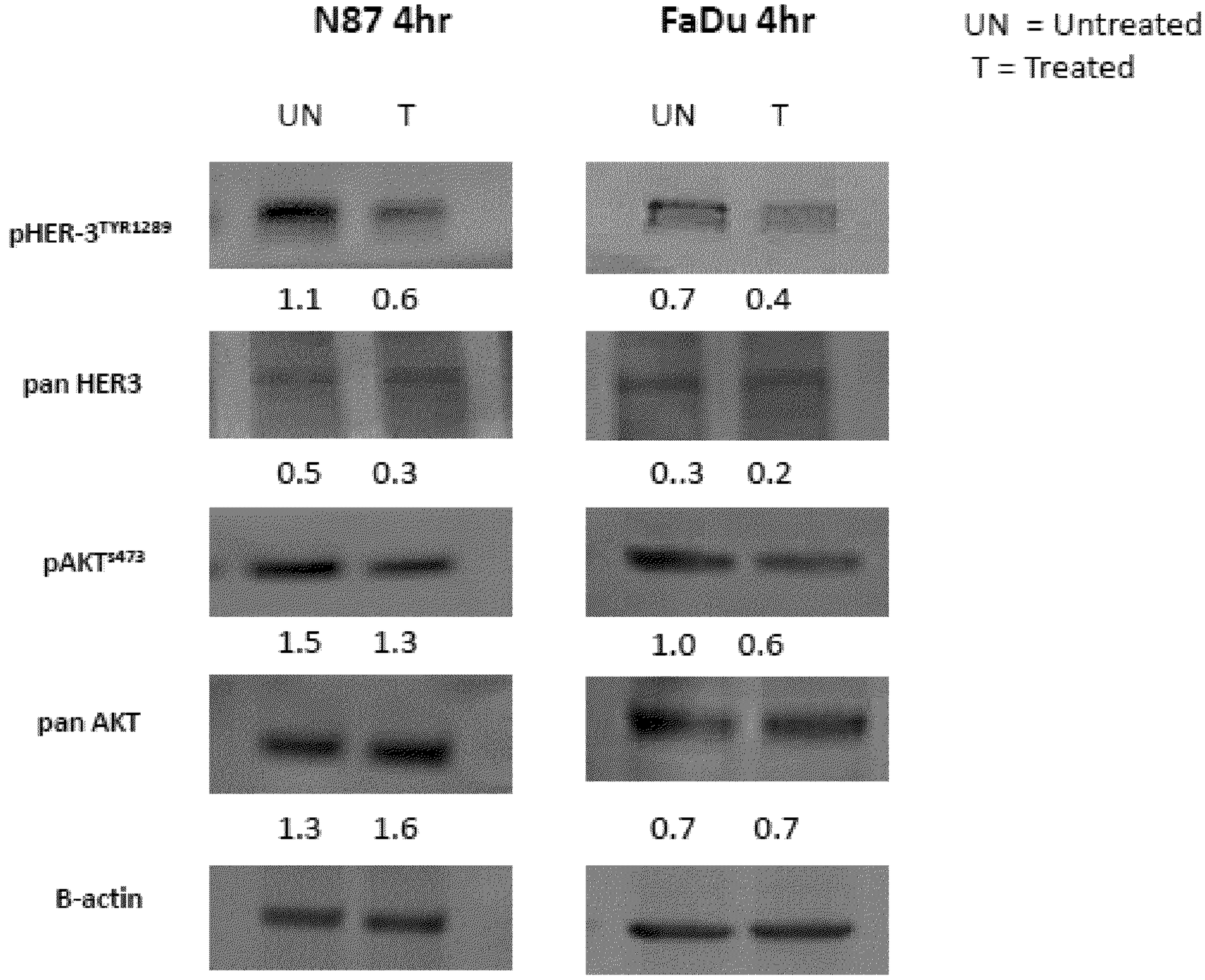

N87 4hr
FaDu 4hr
UN = Untreated
T = Treated
UN T
UN T
pHER-3TYR1289
1.1 0.6
0.7 0.4
pan HER3
0.5 0.3
0..3 0.2
pAKT3473
1.5 1.3
1.0 0.6
pan AKT
1.3 1.6
0.7 0.7
B-actin

Figure 17

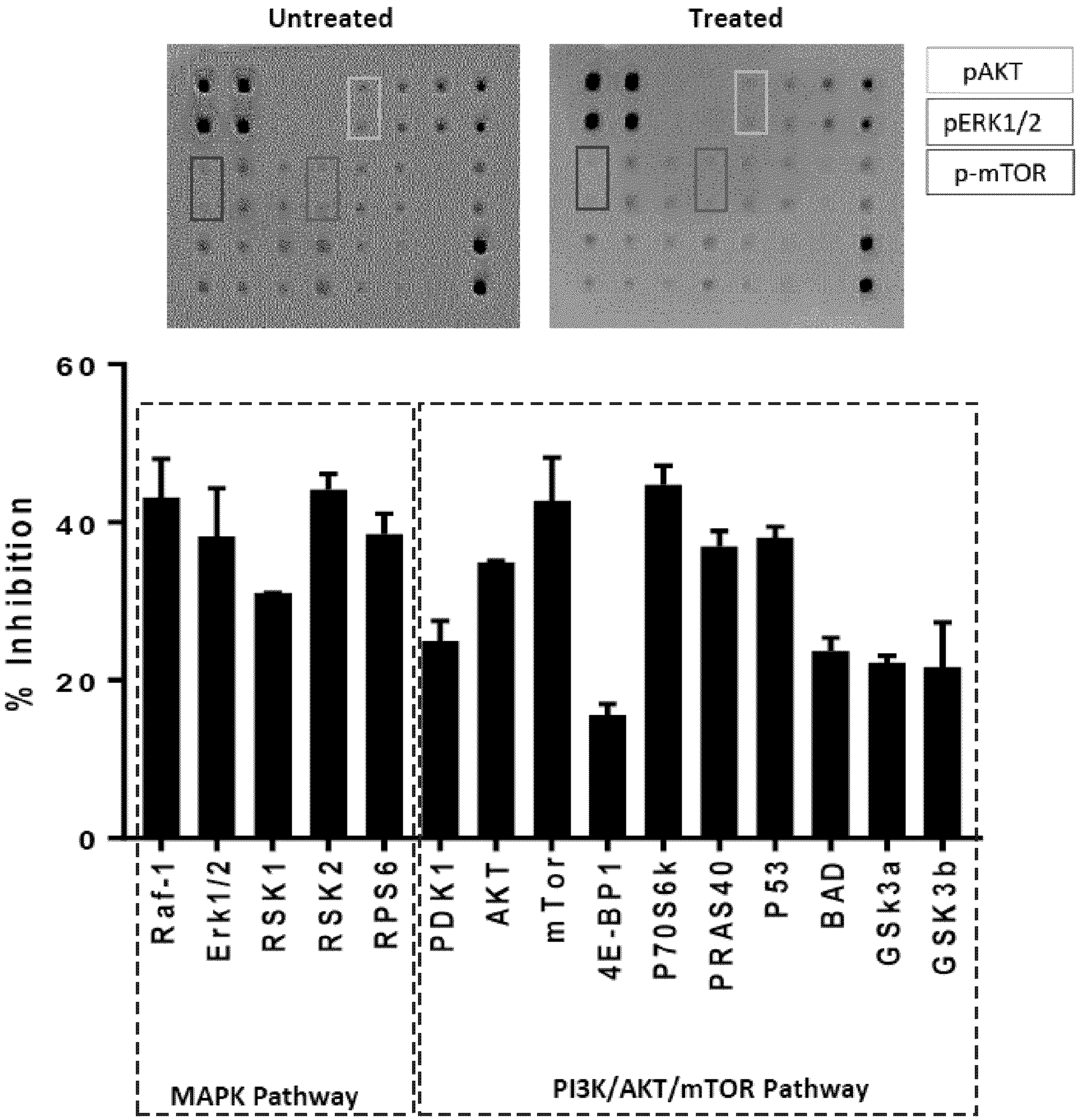

Untreated
Treated
pAKT
pERK1/2
p-mTOR
% Inhibition
60
40
20
0
Raf-1
Erk1/2
RSK1
RSK2
RPS6
PDK1
AKT
mTor
4E-BP1
P70S6k
PRAS40
P53
BAD
GSk3a
GSK3b
MAPK Pathway
PI3K/AKT/mTOR Pathway

Figure 18

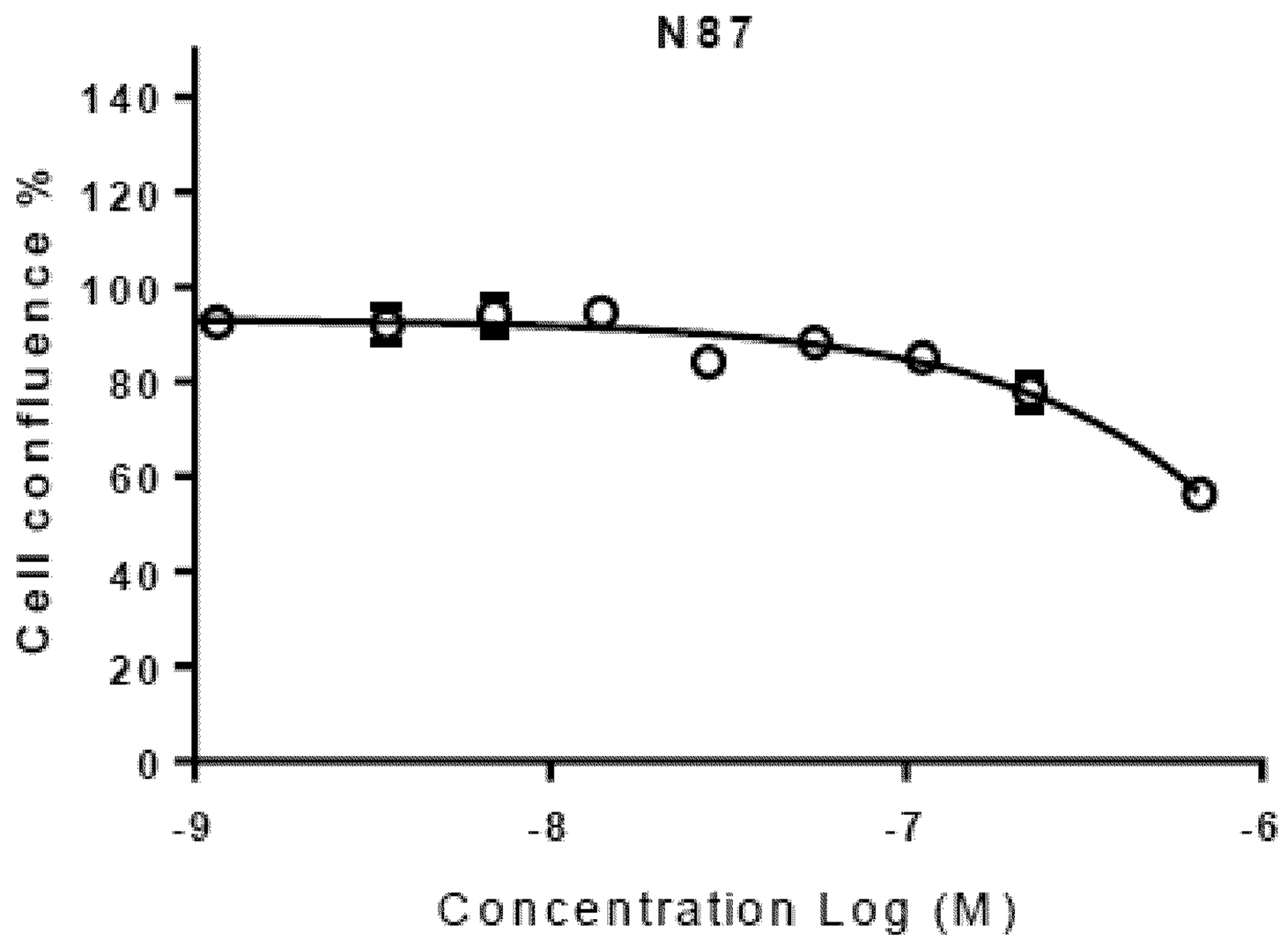


Figure 19A

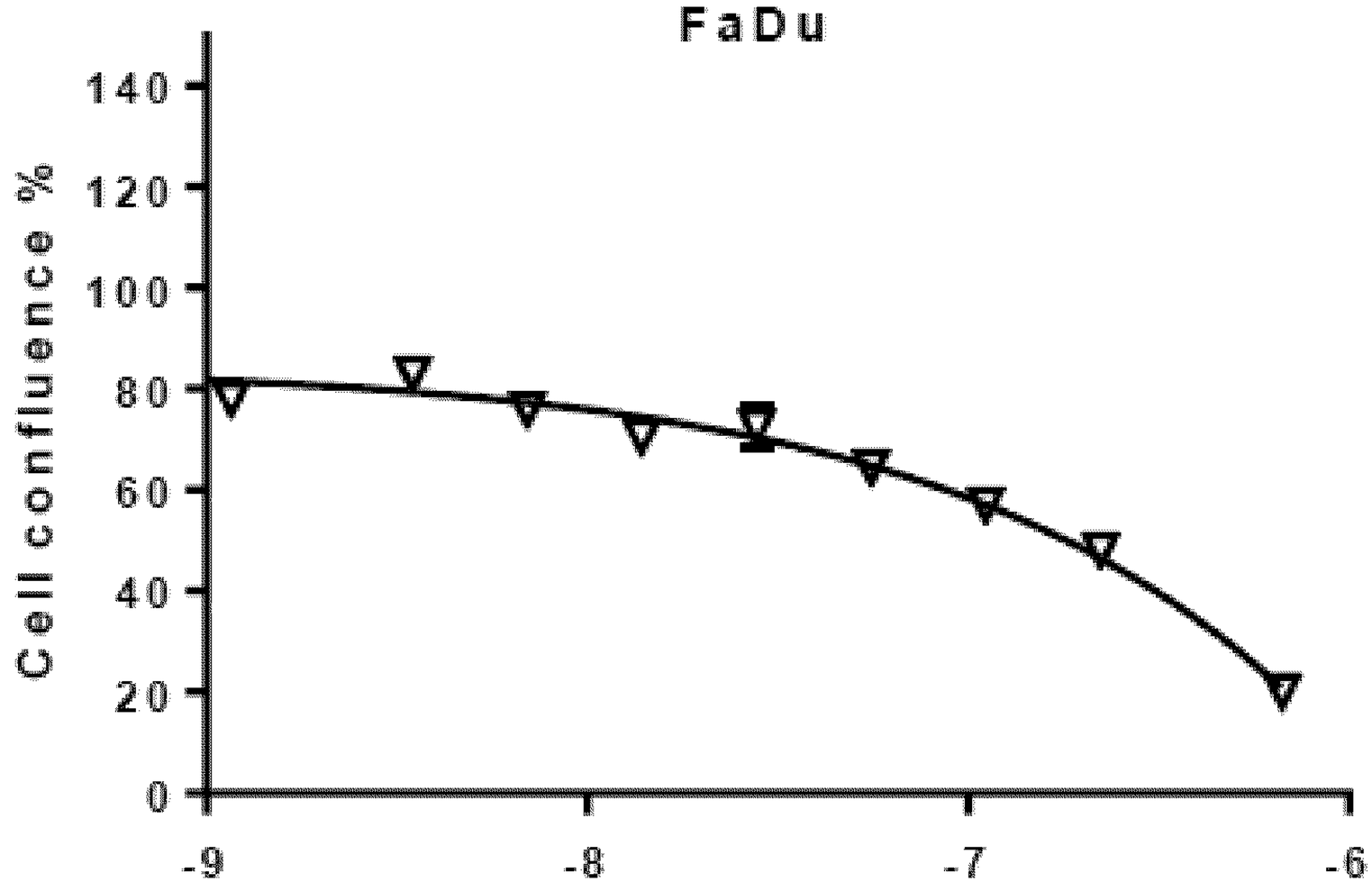


Figure 19B

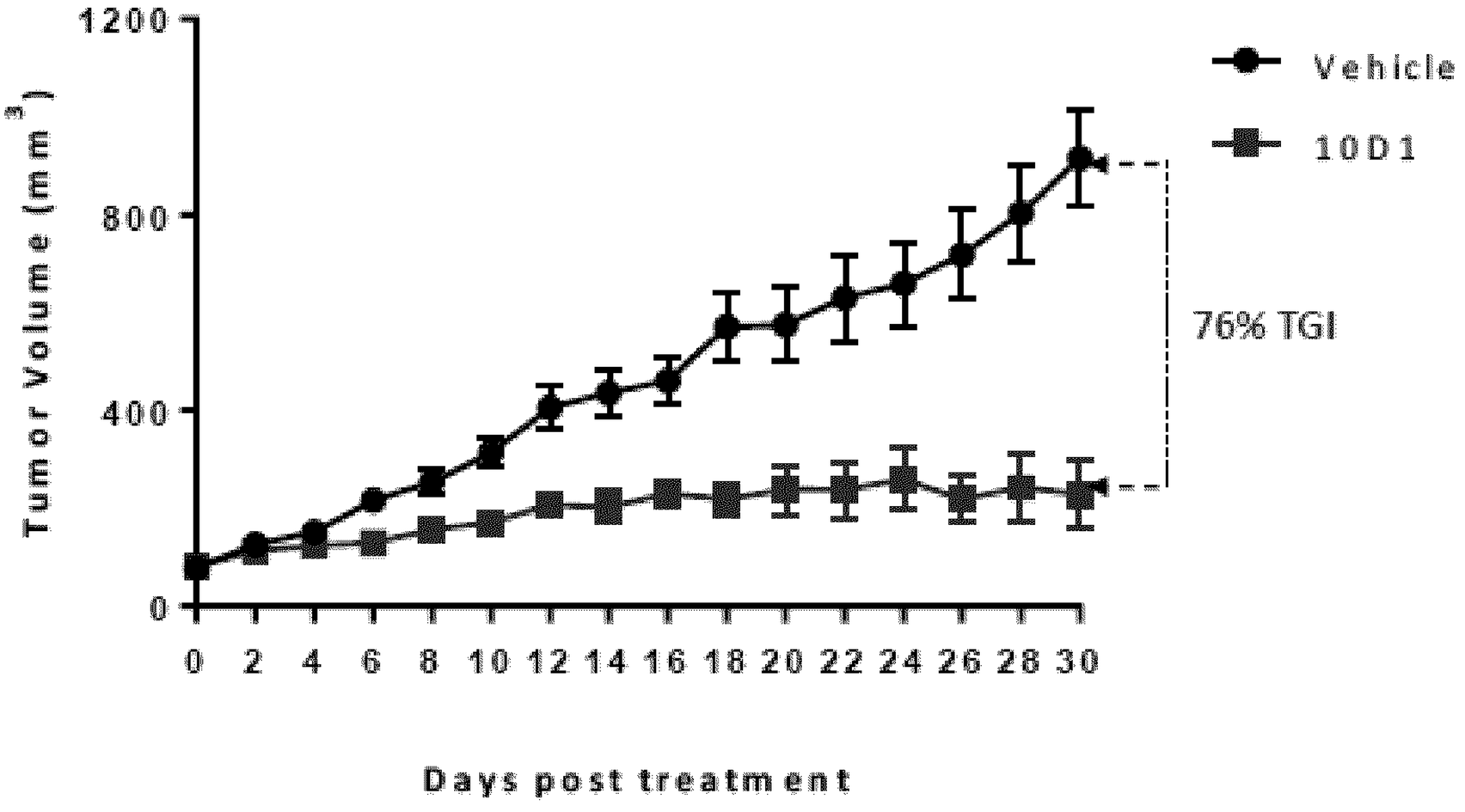


Figure 20

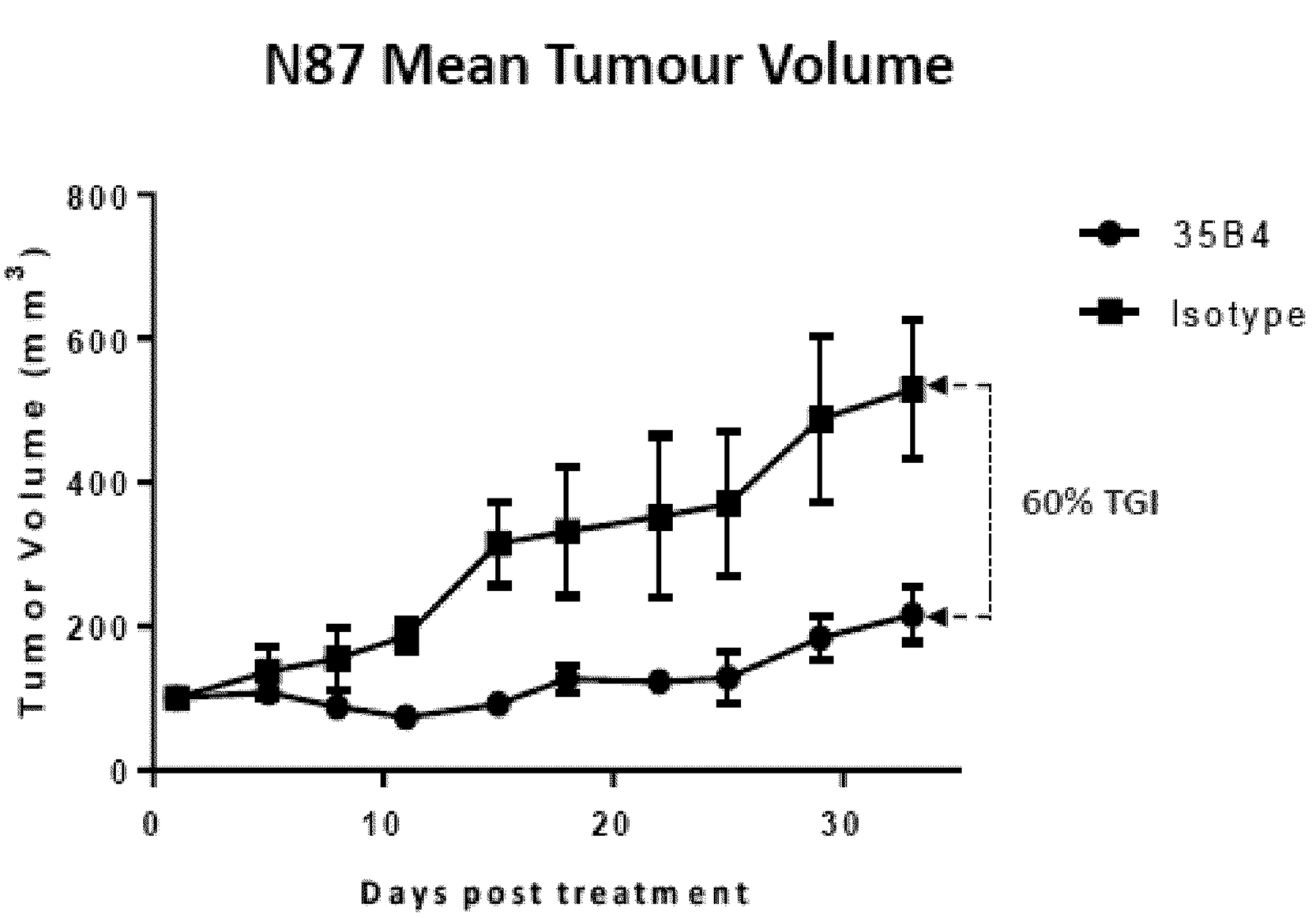


Figure 21

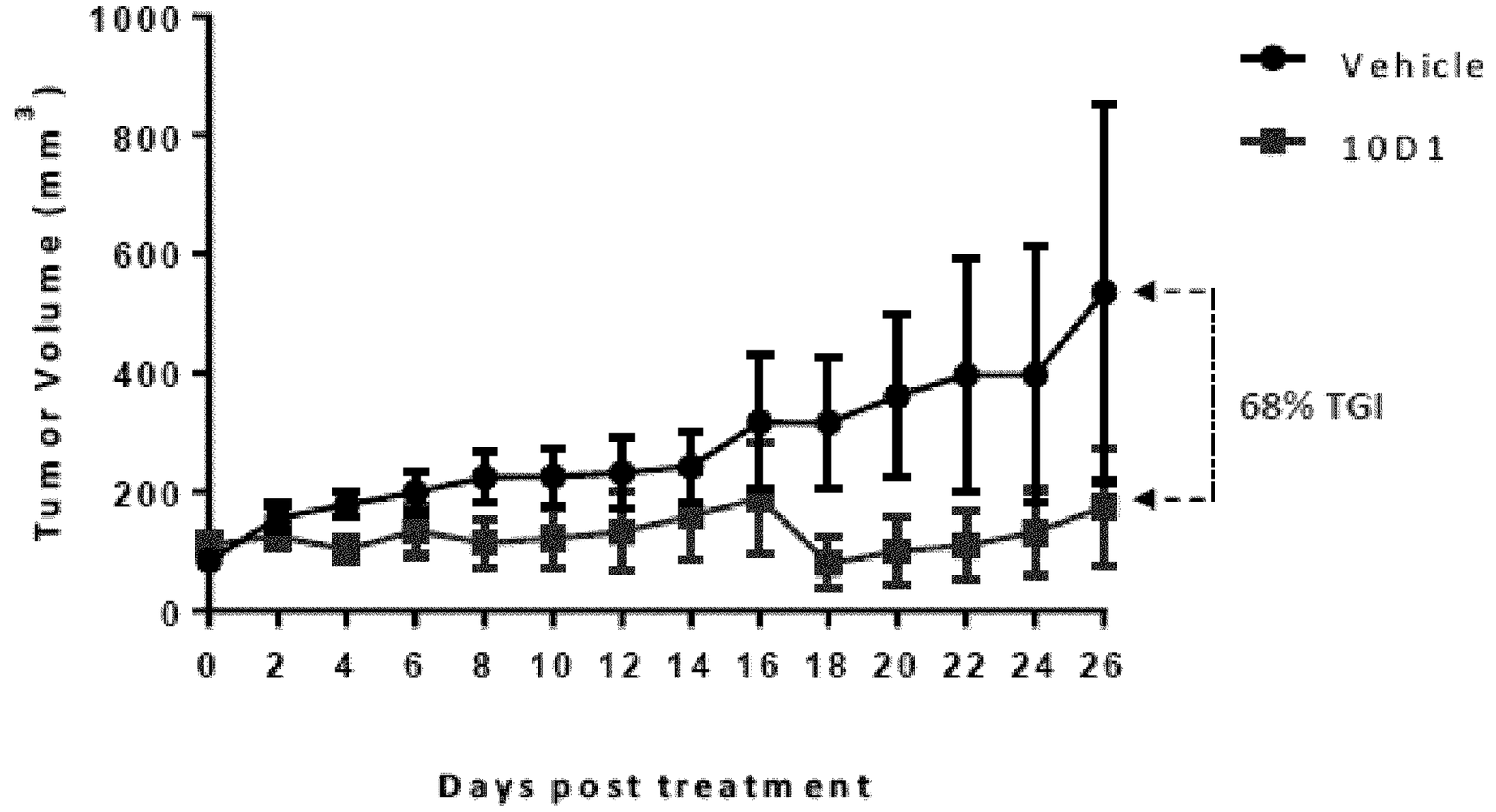


Figure 22

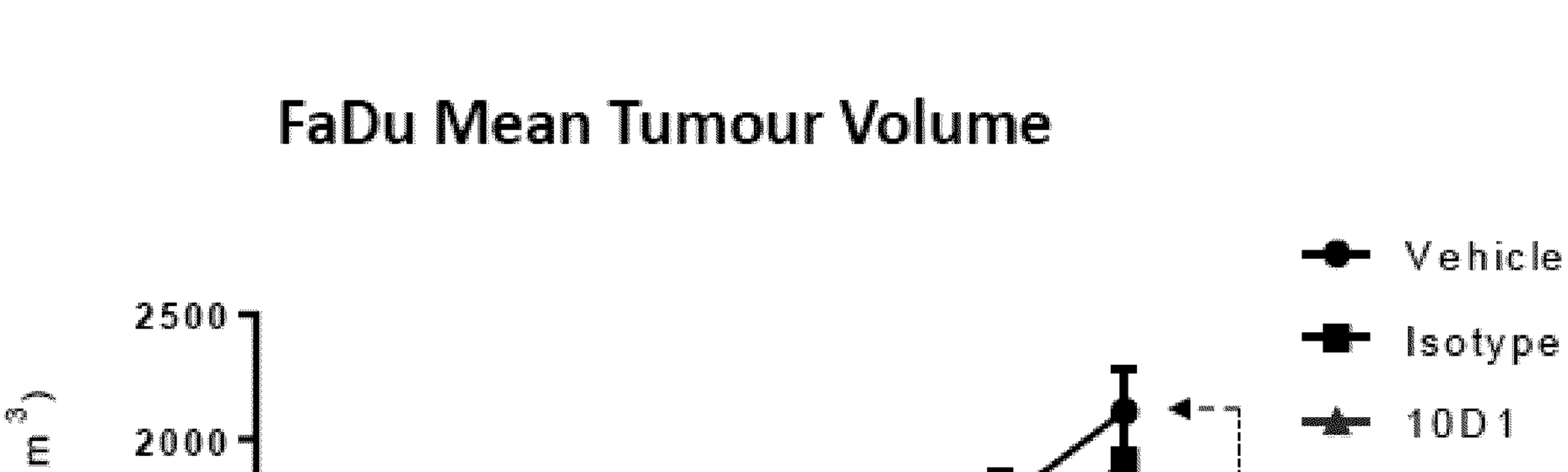


Figure 23

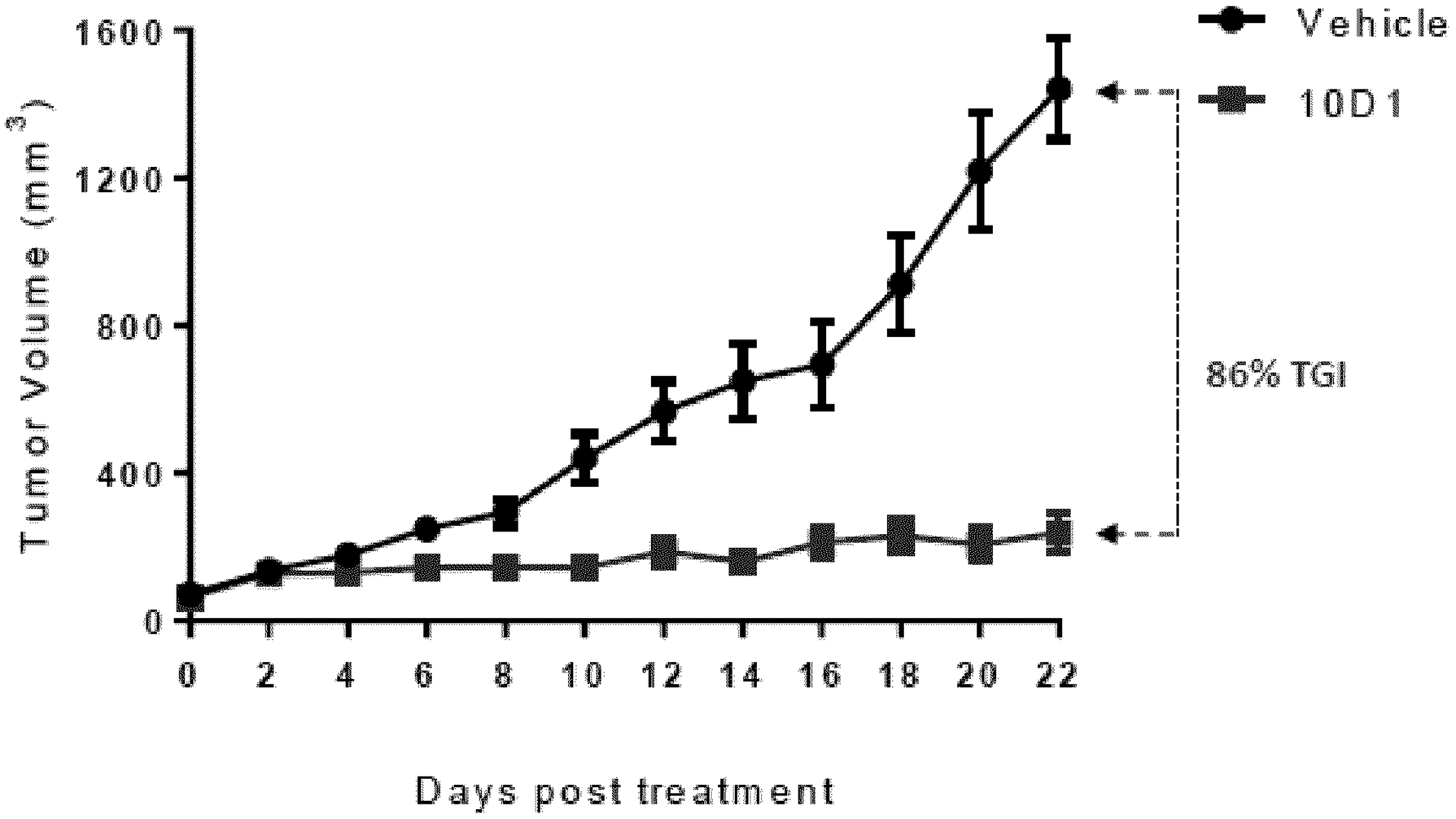


Figure 24

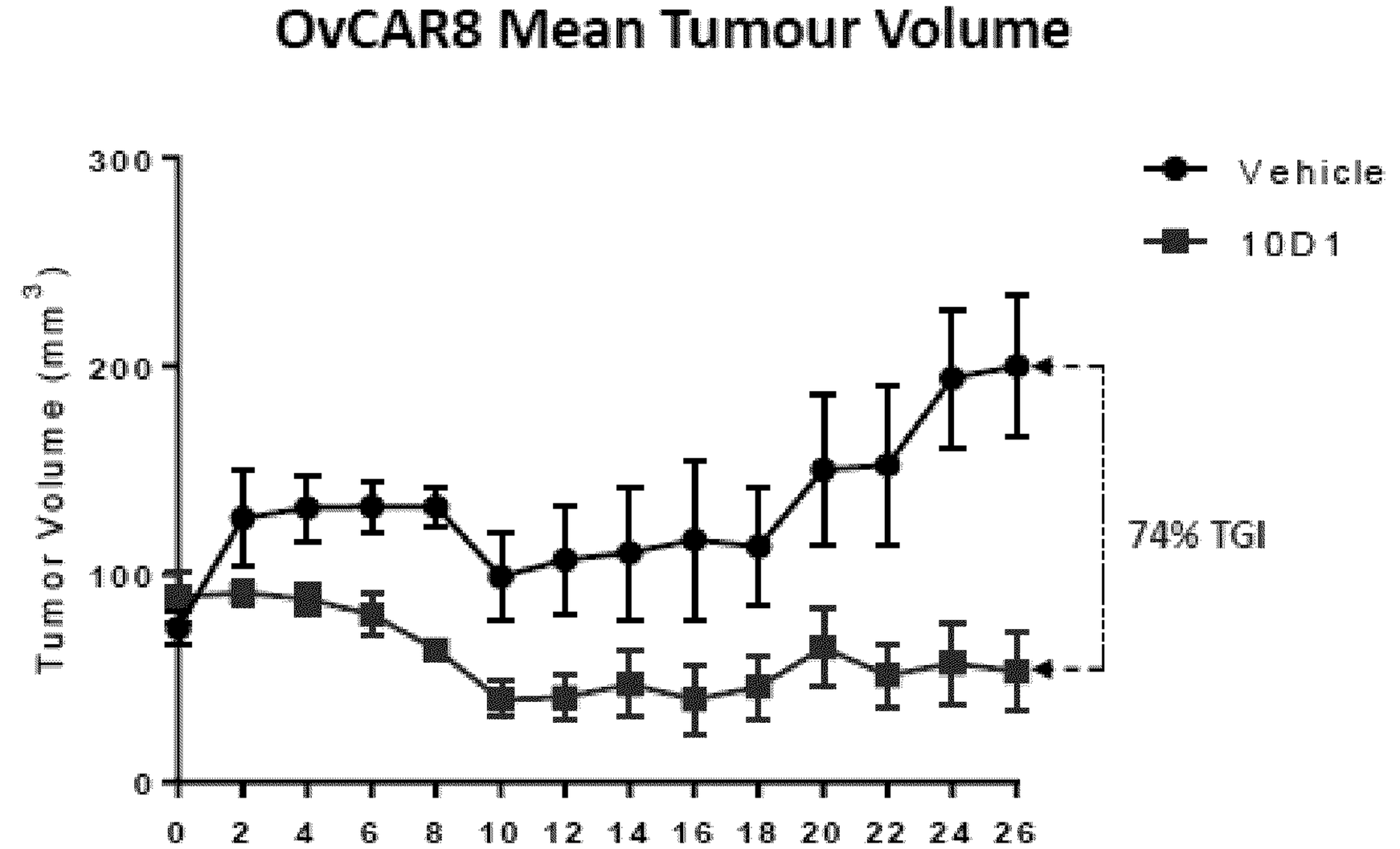


Figure 25

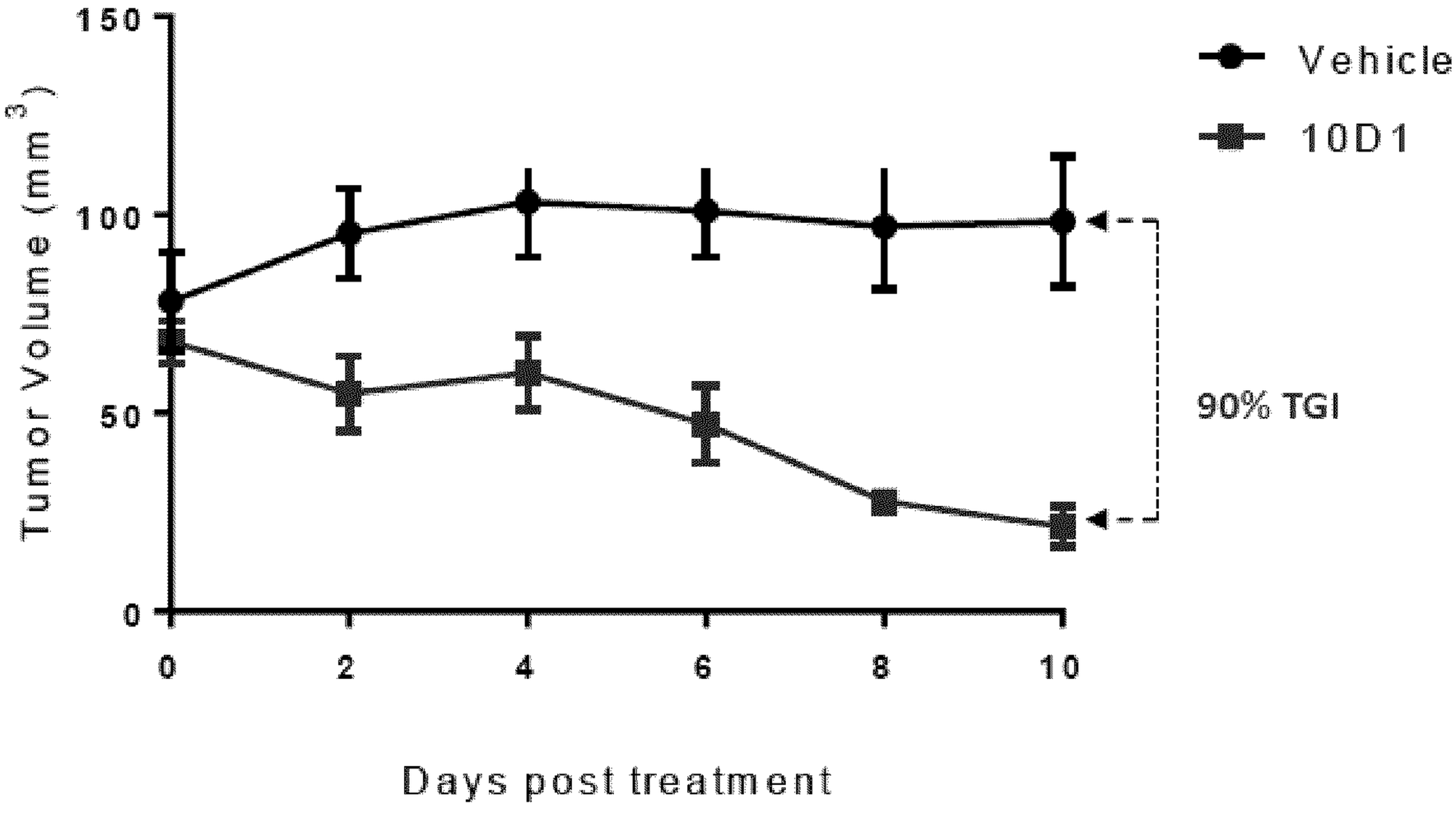


Figure 26

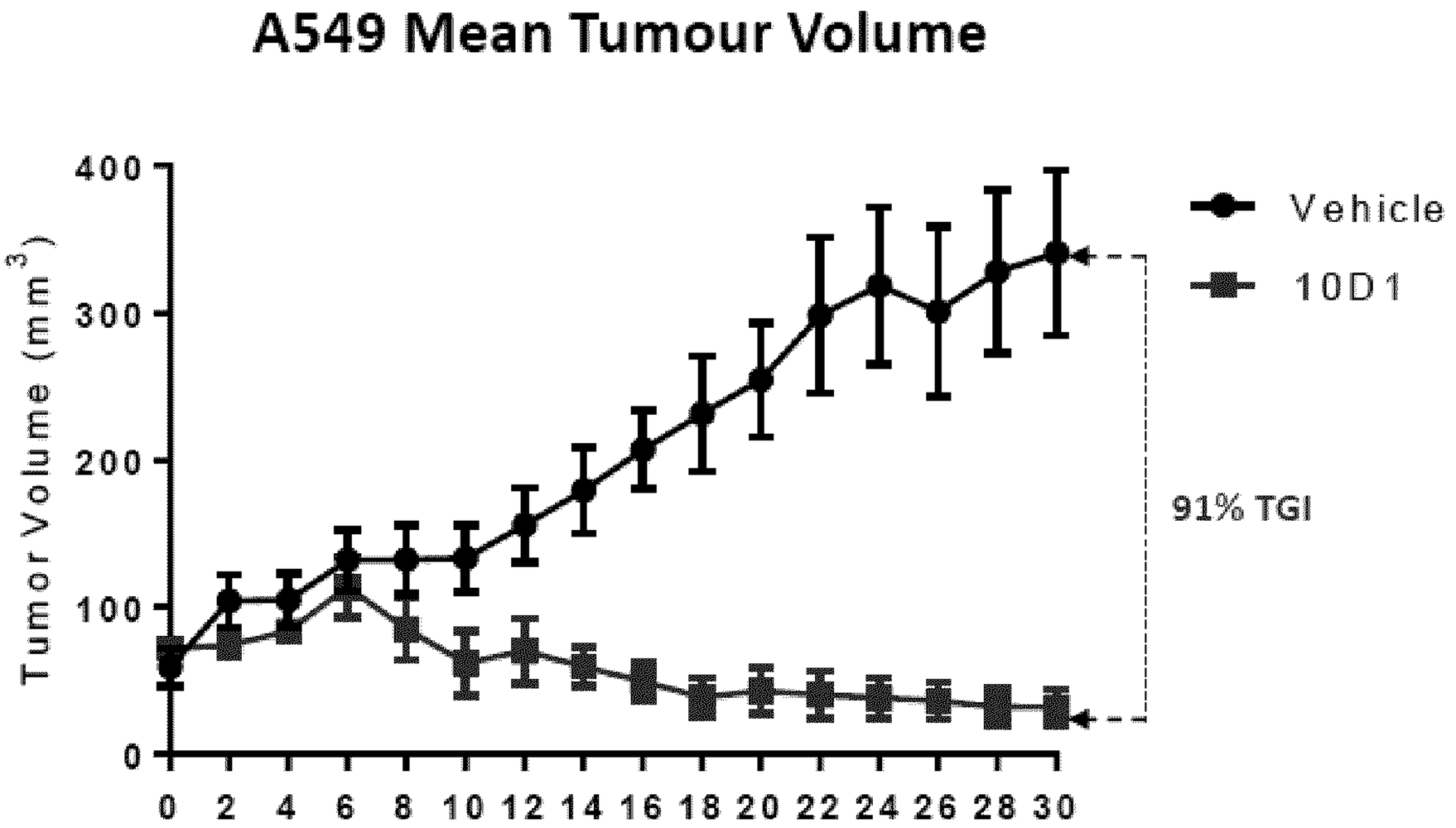


Figure 27

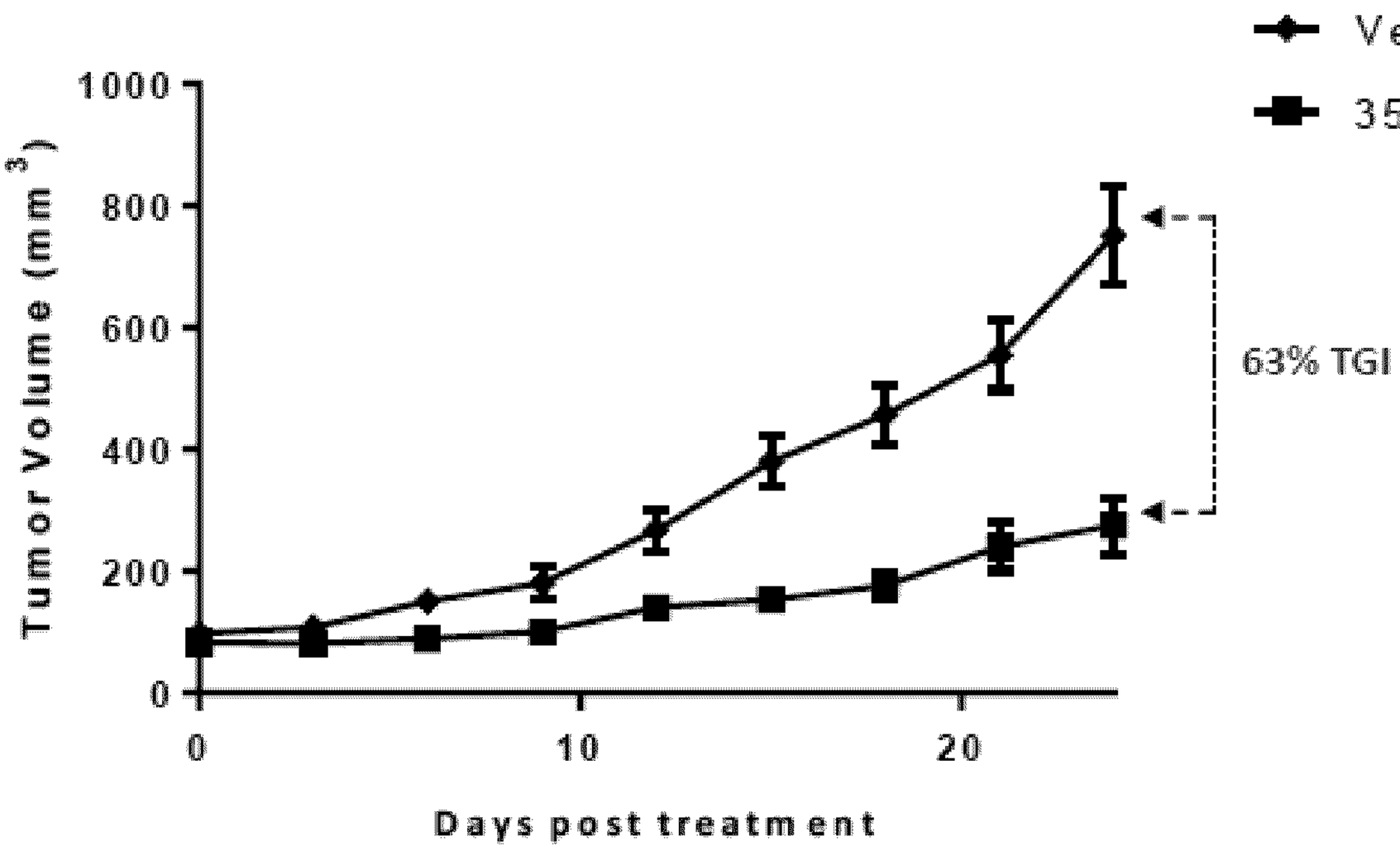


Figure 28

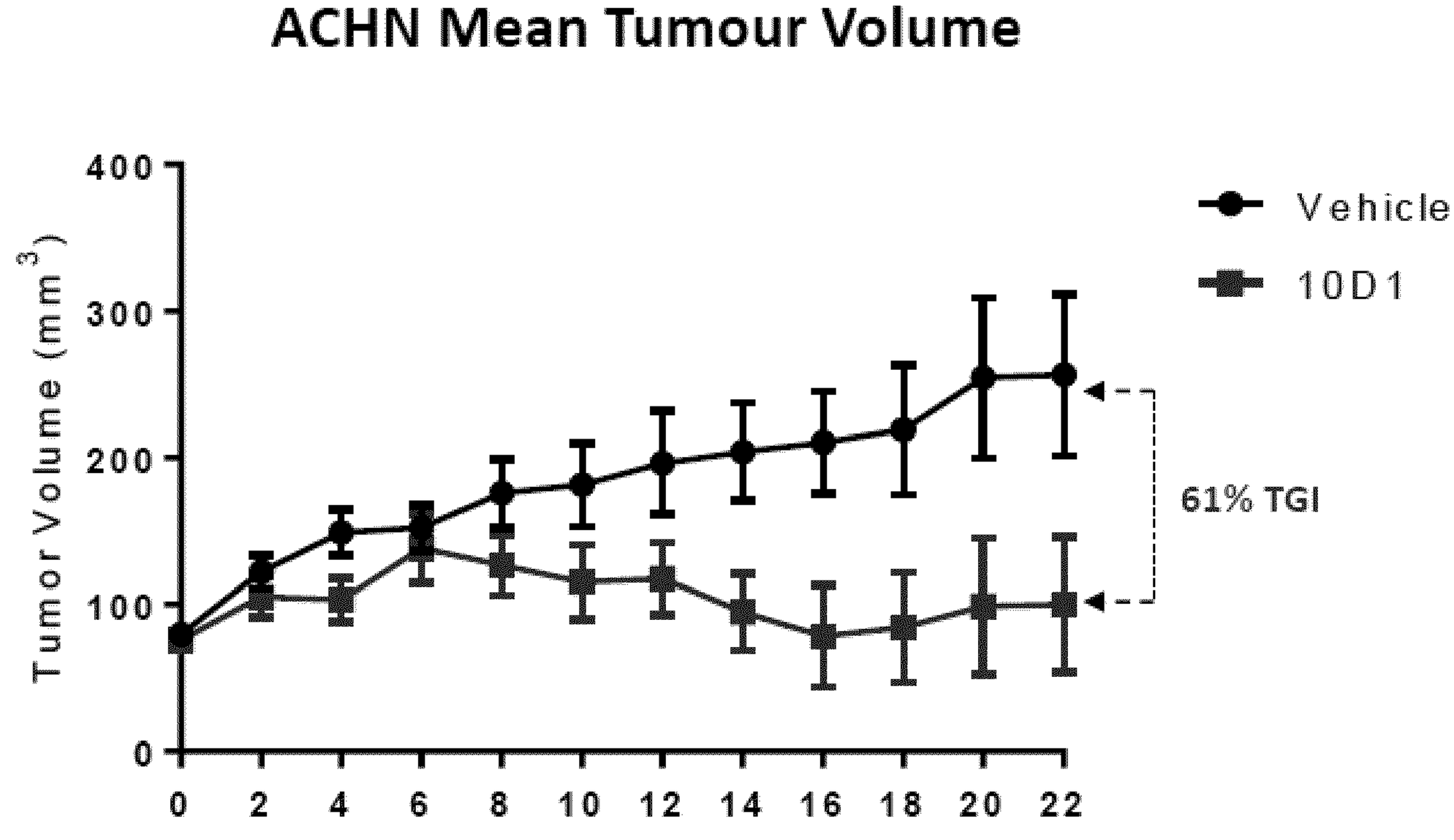
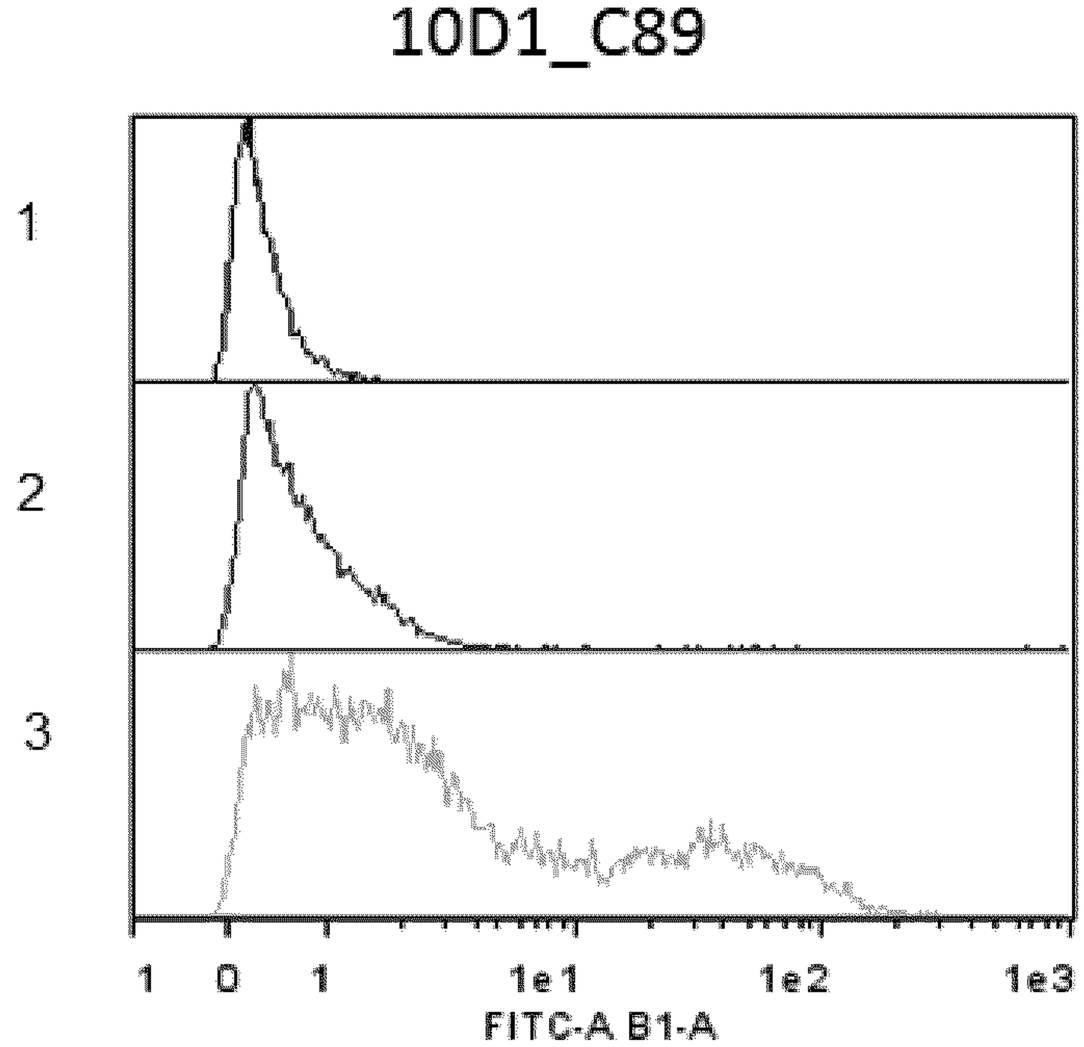
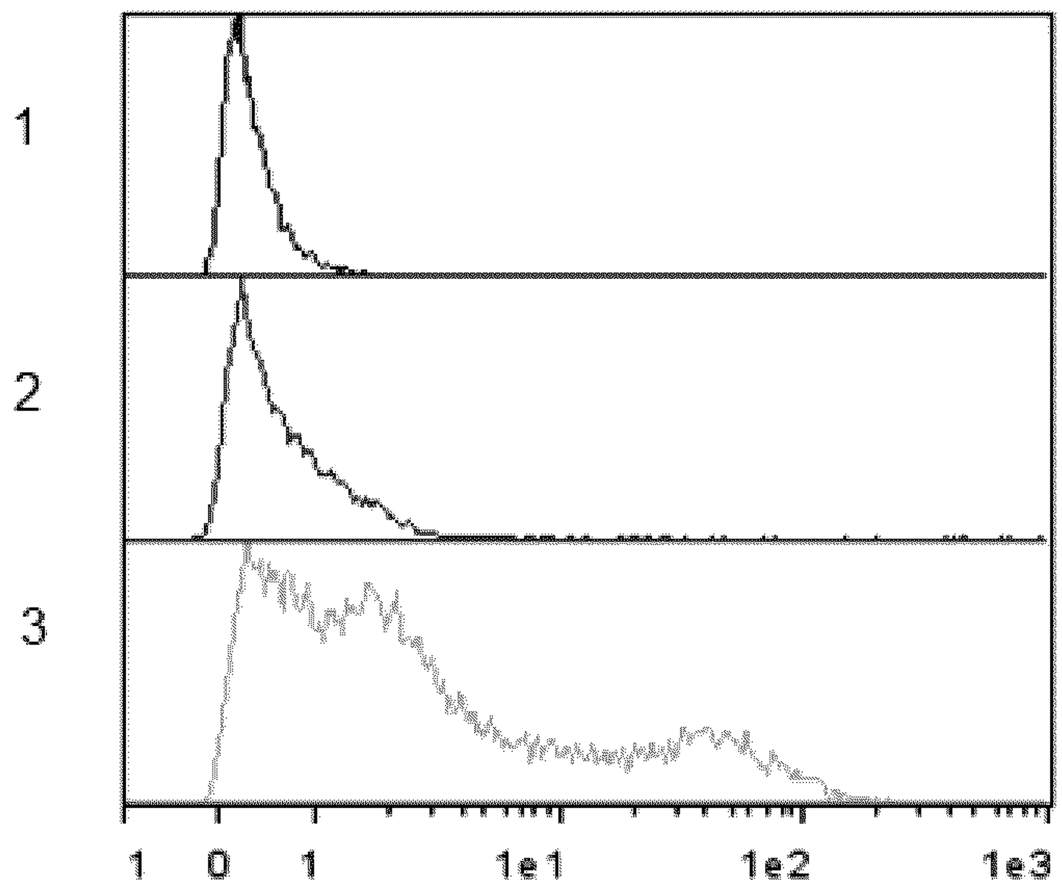


Figure 29



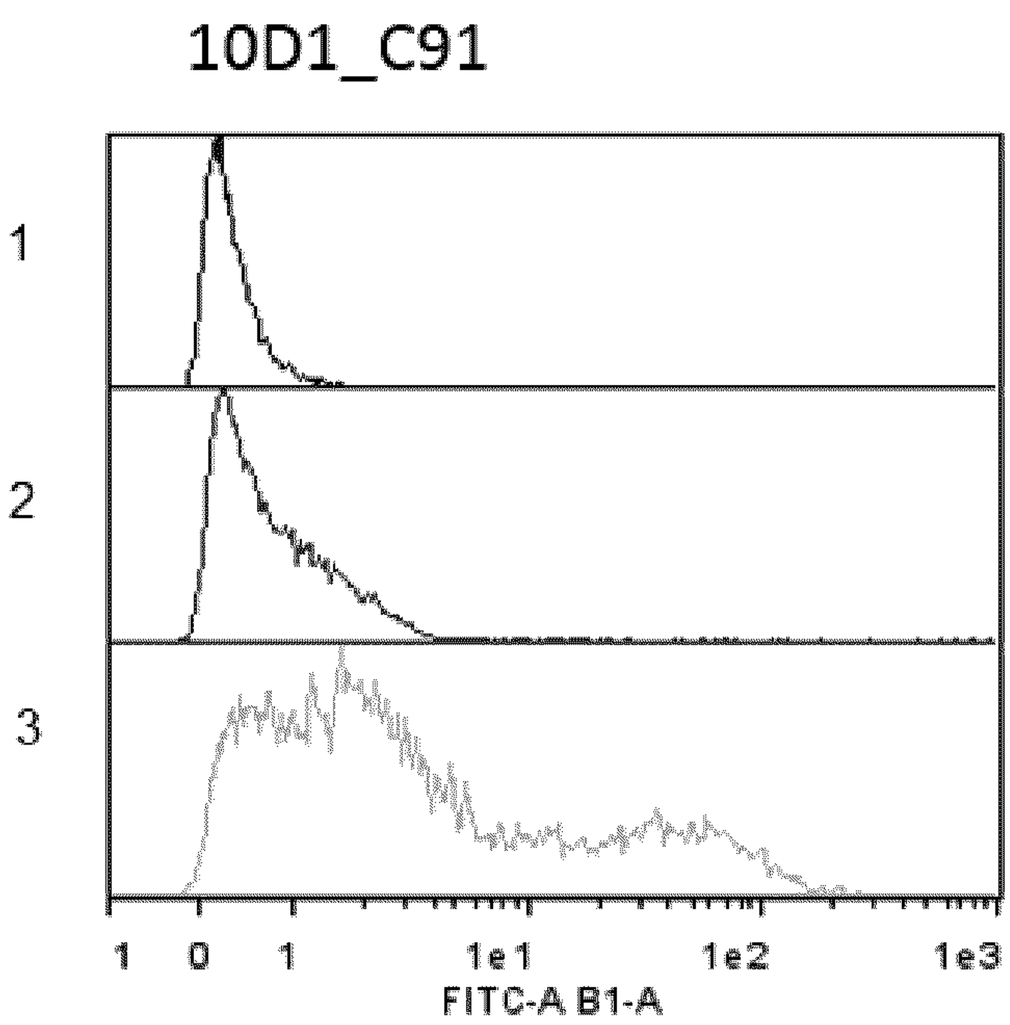
	Color	Population	% Parent
1		HER3 Positive [293_Unstained]	0.14
2		HER3 Positive [293_10D1_C-89Sc]	2.79
3		HER3 Positive [293_OE HER3_10D1_C-89Sc]	44.57

Figure 30



	Color	Population	% Parent
1		HER3 Positive [293_Unstained]	0.14
2		HER3 Positive [293_10D1_C-90Sc]	2.48
3		HER3 Positive [293_OE HER3_10D1_C-90Sc]	41.81

Figure 31



	Color	Population	% Parent
1		HER3 Positive [293_Unstained]	0.14
2		HER3 Positive [293_10D1_C-91Sc]	5.38
3		HER3 Positive [293_OE HER3_10D1_C-91Sc]	48.05

Figure 32

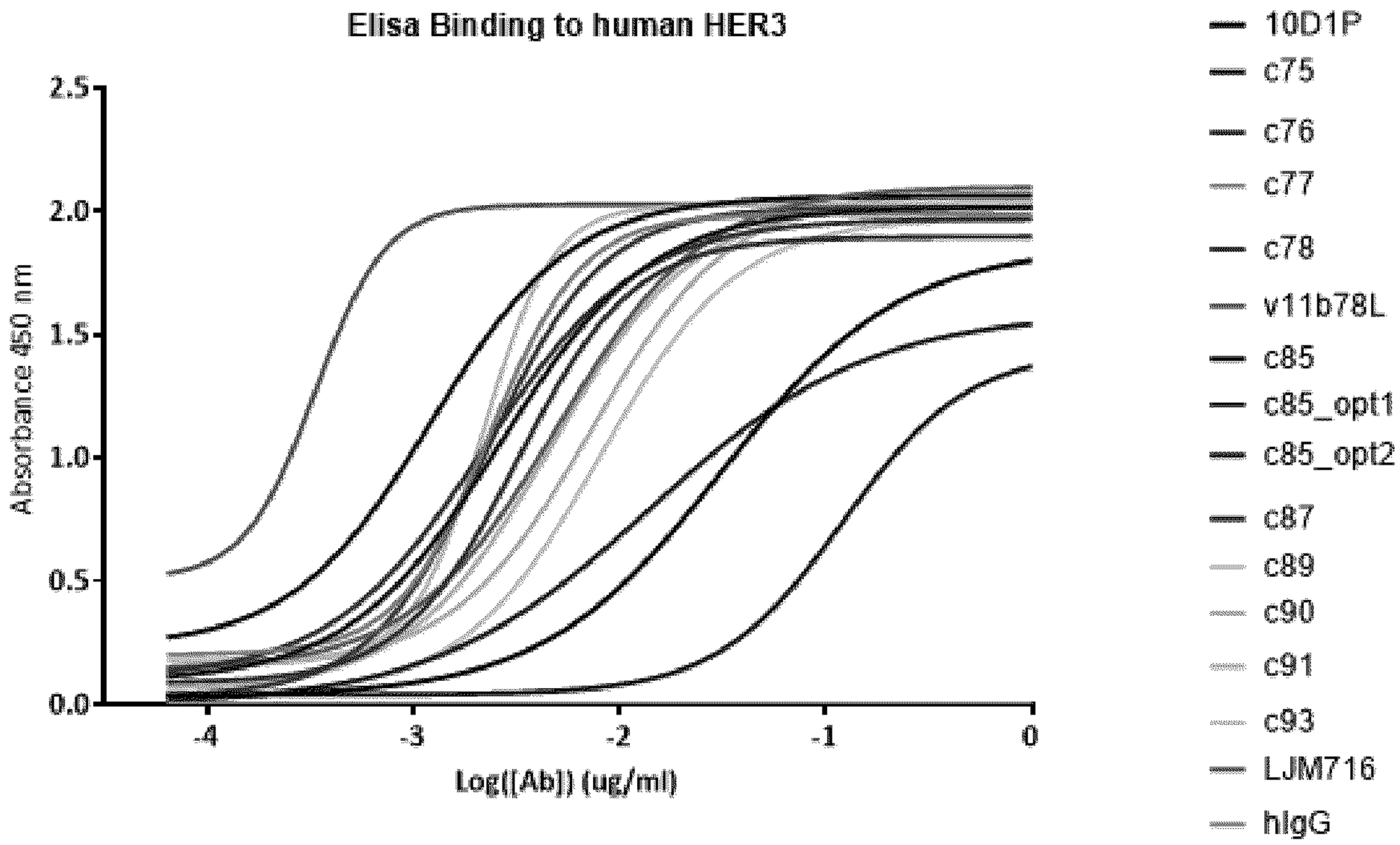


Figure 33A

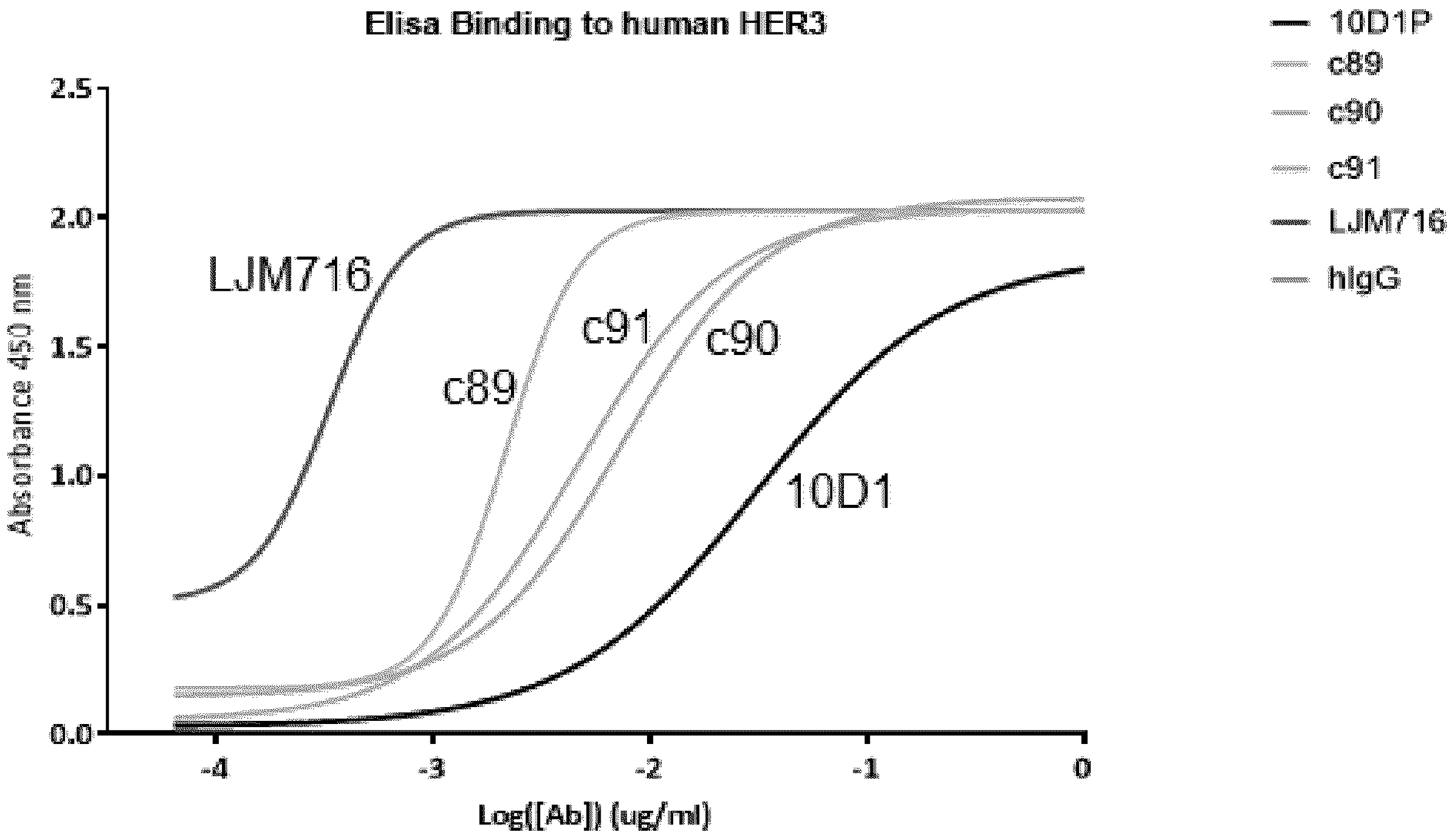


Figure 33B

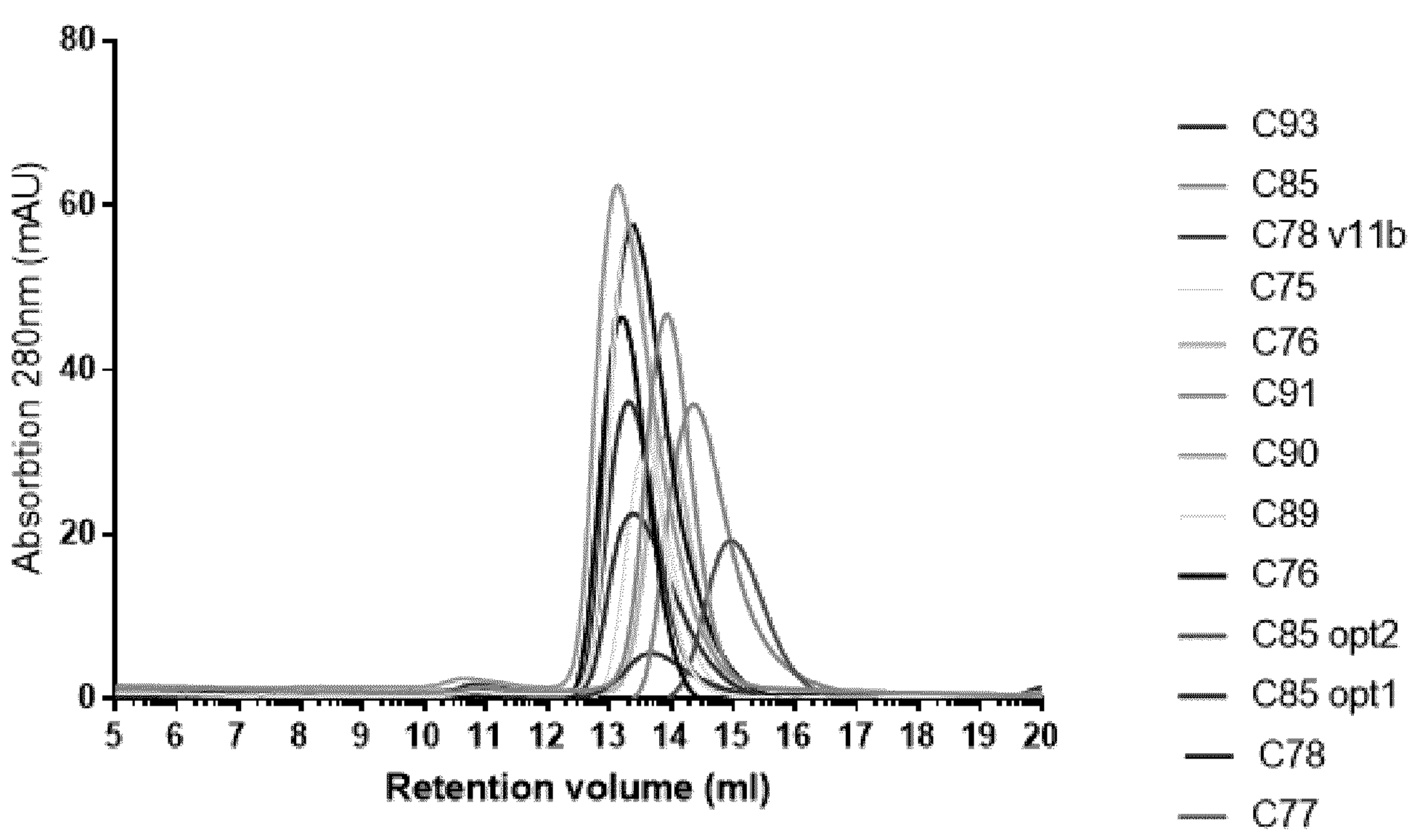


Figure 34A

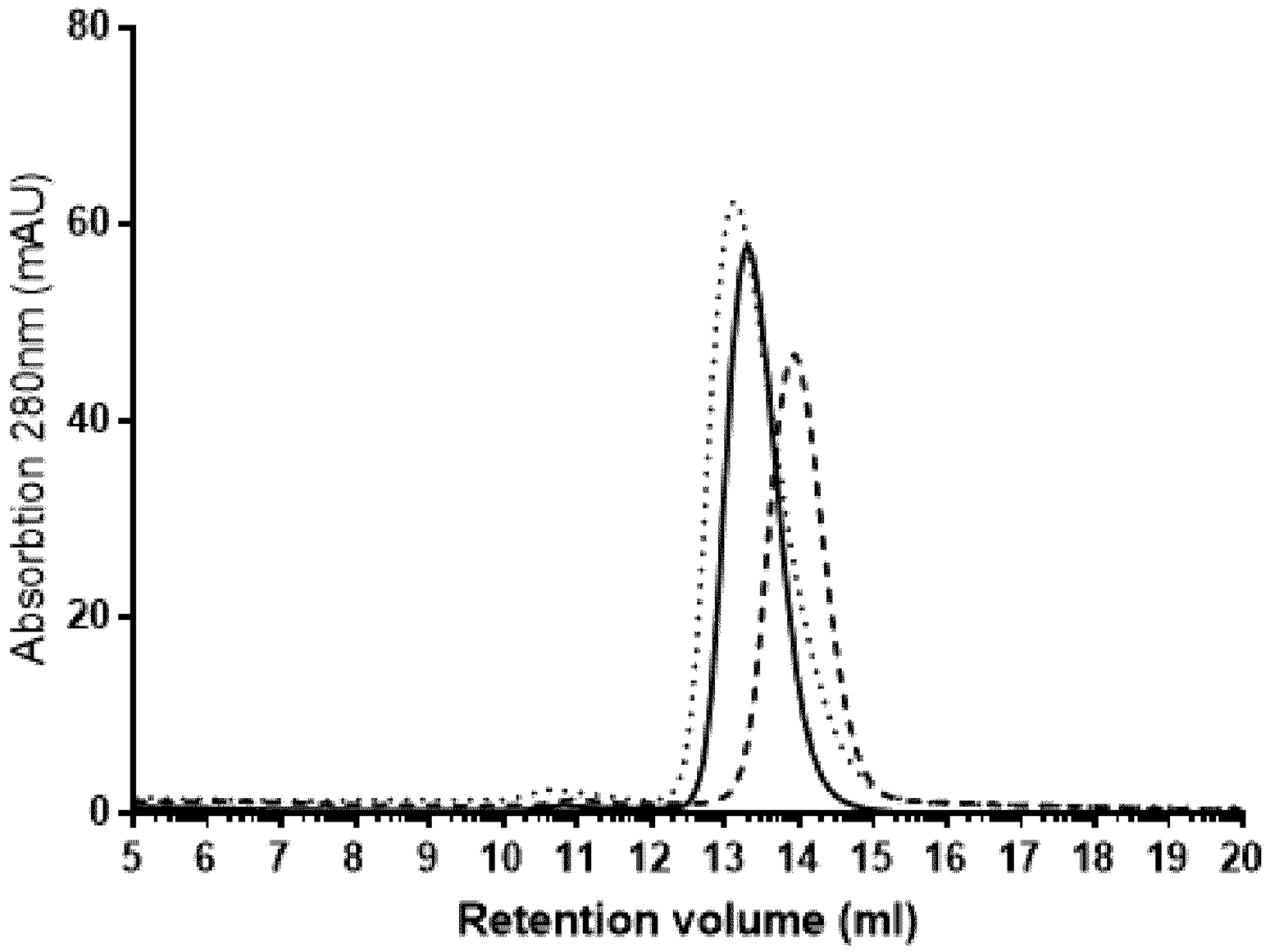

C91
C90
C89
Absorbtion 280nm (mAU)
0
20
40
60
80
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
Retention volume (ml)

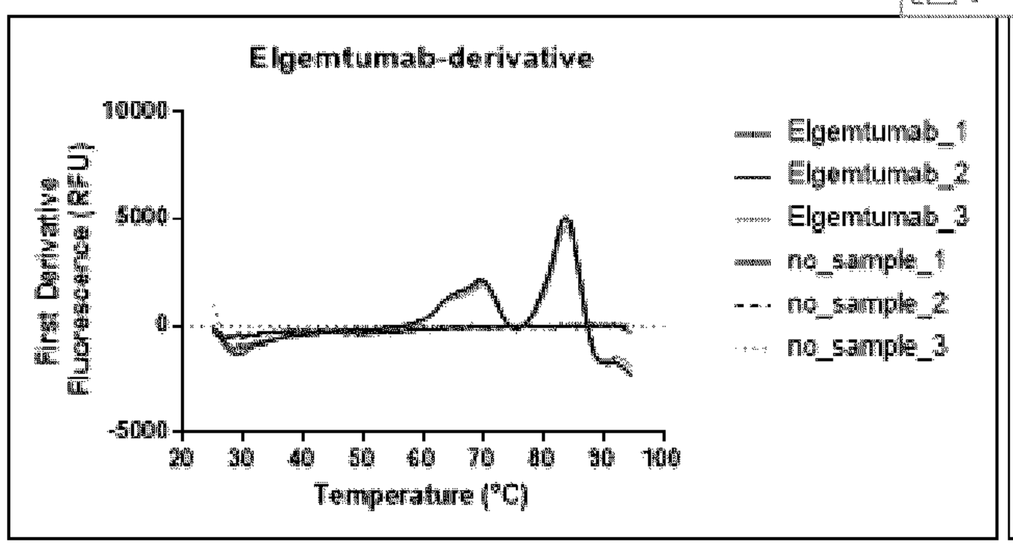
Figure 34B

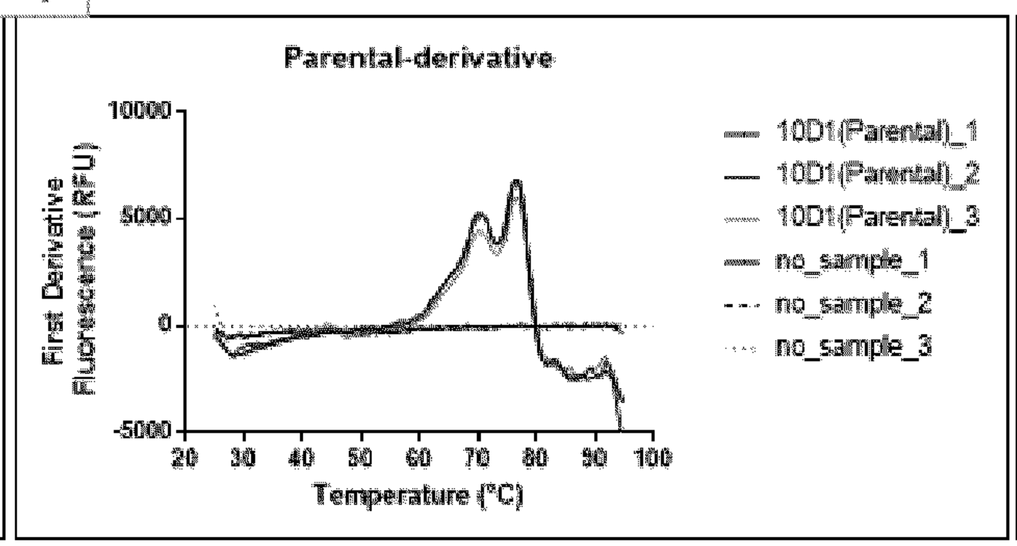
	Tm1 (°C)	Tm2 (°C)
LM716	70.8	83.8

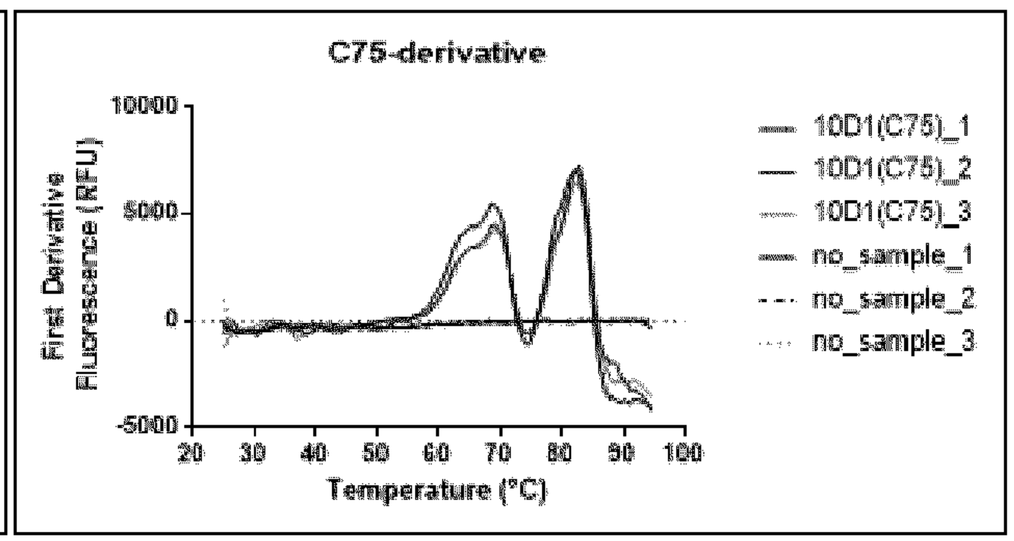
	Tm1 (°C)	Tm2 (°C)
10D1 (Parental)	69.9	77.2

	Tm1 (°C)	Tm2 (°C)
10D1 (C75)	69.5	82.6

(Ctrl)



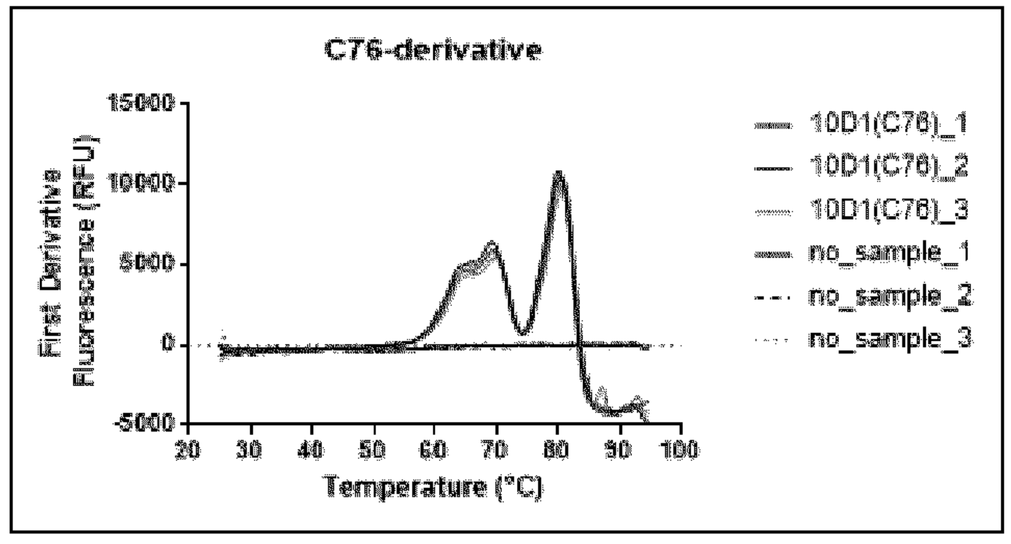


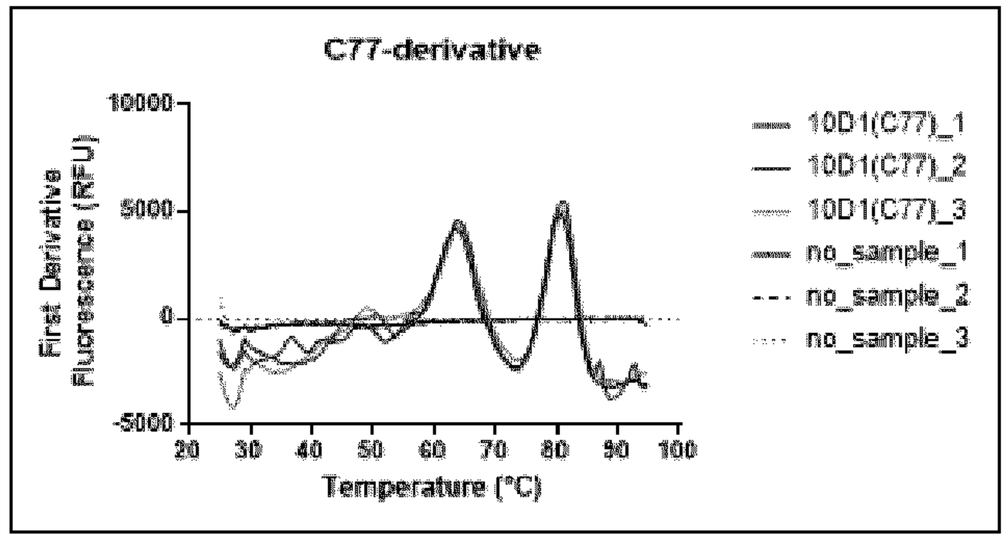


	Tm1 (°C)	Tm2 (°C)
10D1 (C76)	69.6	80.9

	Tm1 (°C)	Tm2 (°C)
10D1 (C77)	64.1	80.9

	Tm1 (°C)	Tm2 (°C)
10D1 (C78)	70.2	83.3





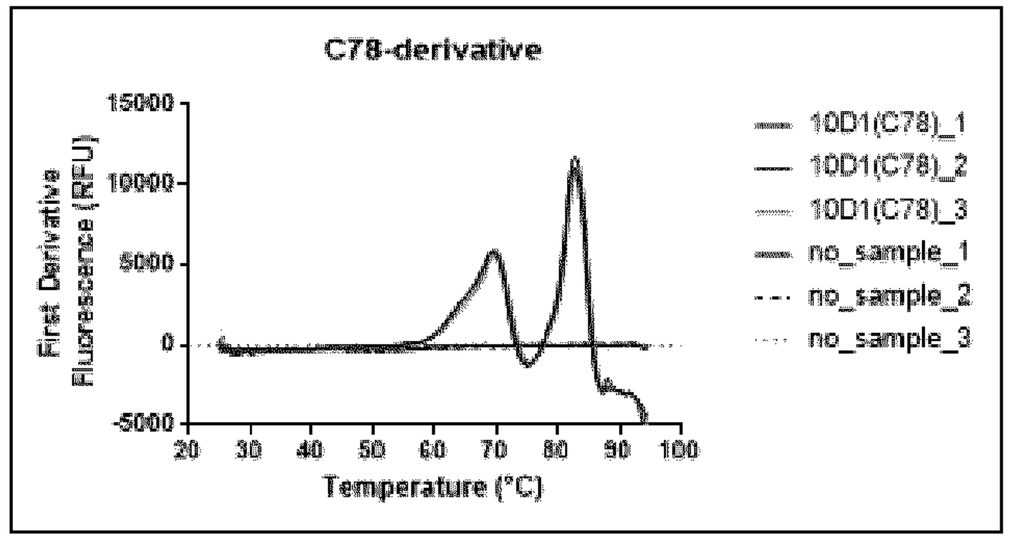


Figure 35A

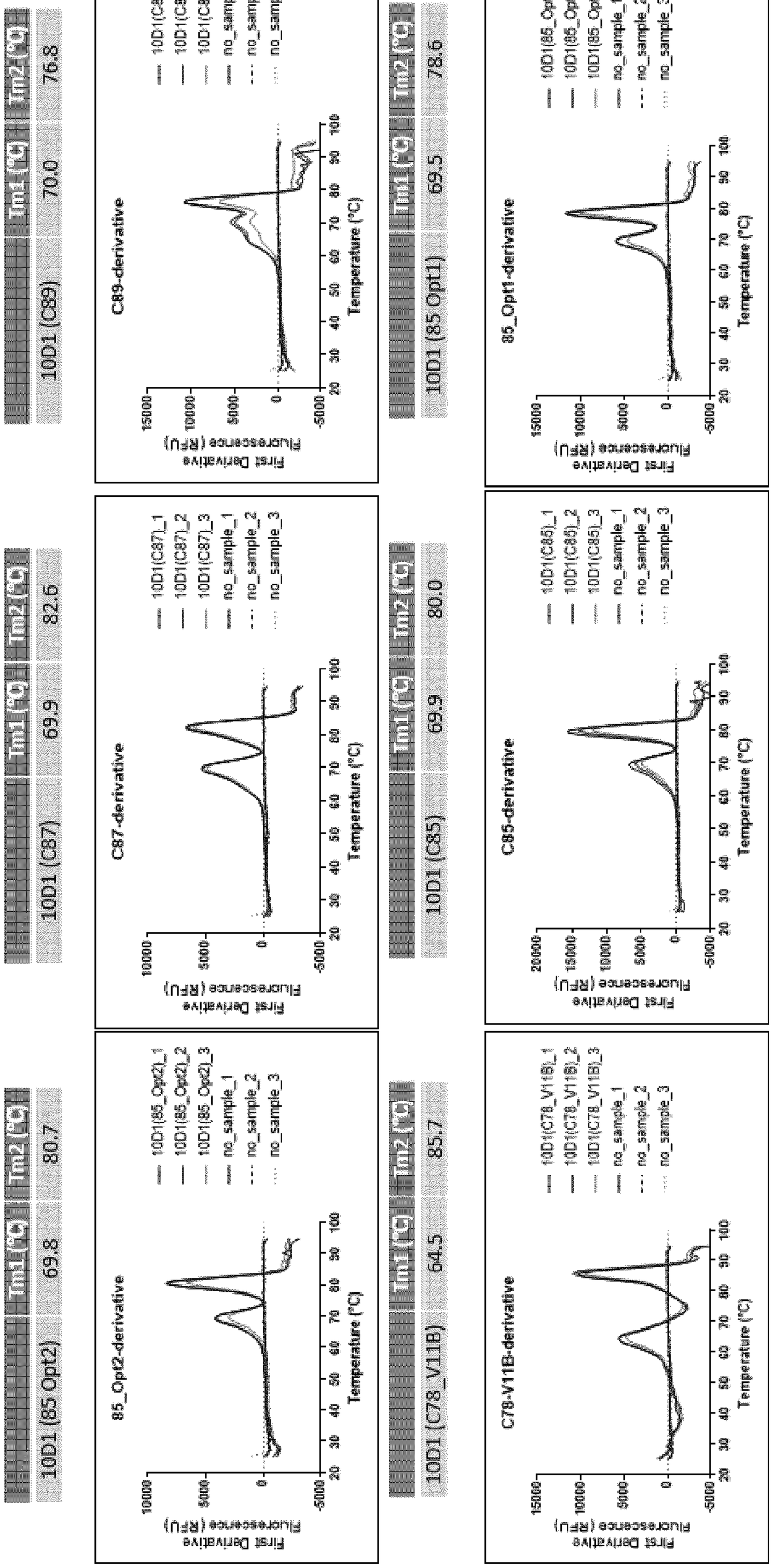

10D1(C89)_1
10D1(C89)_2
10D1(C89)_3
no_sample_1
no_sample_2
no_sample_3
C89-derivative
First Derivative Fluorescence (RFU)
Temperature (°C)
Tm1 (°C) | Tm2 (°C)
70.0 | 79.8
10D1 (C89)
10D1(85_Opt1)_1
10D1(85_Opt1)_2
10D1(85_Opt1)_3
no_sample_1
no_sample_2
no_sample_3
85_Opt1-derivative
First Derivative Fluorescence (RFU)
Temperature (°C)
Tm1 (°C) | Tm2 (°C)
69.5 | 78.6
10D1 (85 Opt1)
10D1(C87)_1
10D1(C87)_2
10D1(C87)_3
no_sample_1
no_sample_2
no_sample_3
C87-derivative
First Derivative Fluorescence (RFU)
Temperature (°C)
Tm1 (°C) | Tm2 (°C)
69.9 | 82.6
10D1 (C87)
10D1(85_Opt2)_1
10D1(85_Opt2)_2
10D1(85_Opt2)_3
no_sample_1
no_sample_2
no_sample_3
85_Opt2-derivative
First Derivative Fluorescence (RFU)
Temperature (°C)
Tm1 (°C) | Tm2 (°C)
69.8 | 80.7
10D1 (85 Opt2)
10D1(C85)_1
10D1(C85)_2
10D1(C85)_3
no_sample_1
no_sample_2
no_sample_3
C85-derivative
First Derivative Fluorescence (RFU)
Temperature (°C)
Tm1 (°C) | Tm2 (°C)
69.9 | 80.0
10D1 (C85)
10D1(C78_V11B)_1
10D1(C78_V11B)_2
10D1(C78_V11B)_3
no_sample_1
no_sample_2
no_sample_3
C78-V11B-derivative
First Derivative Fluorescence (RFU)
Temperature (°C)
Tm1 (°C) | Tm2 (°C)
64.5 | 85.7
10D1 (C78_V11B)

Figure 35B

	Tm1 (°C)	Tm2 (°C)
10D1 (C93)	70.0	87.7
10D1 (C91)	74.3	
10D1 (C90)	73.6	
10D1	70.5	

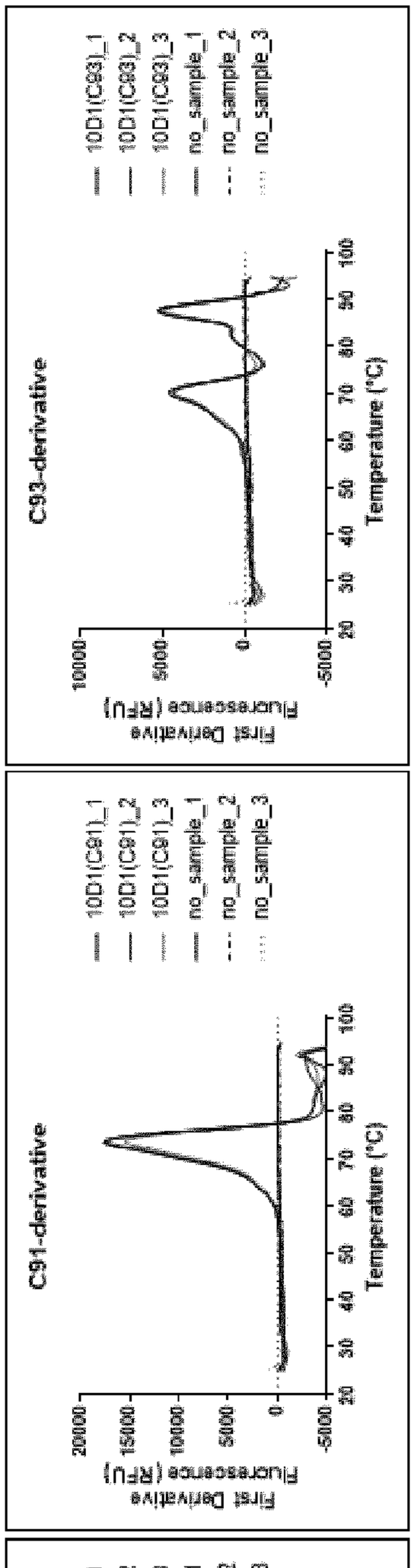
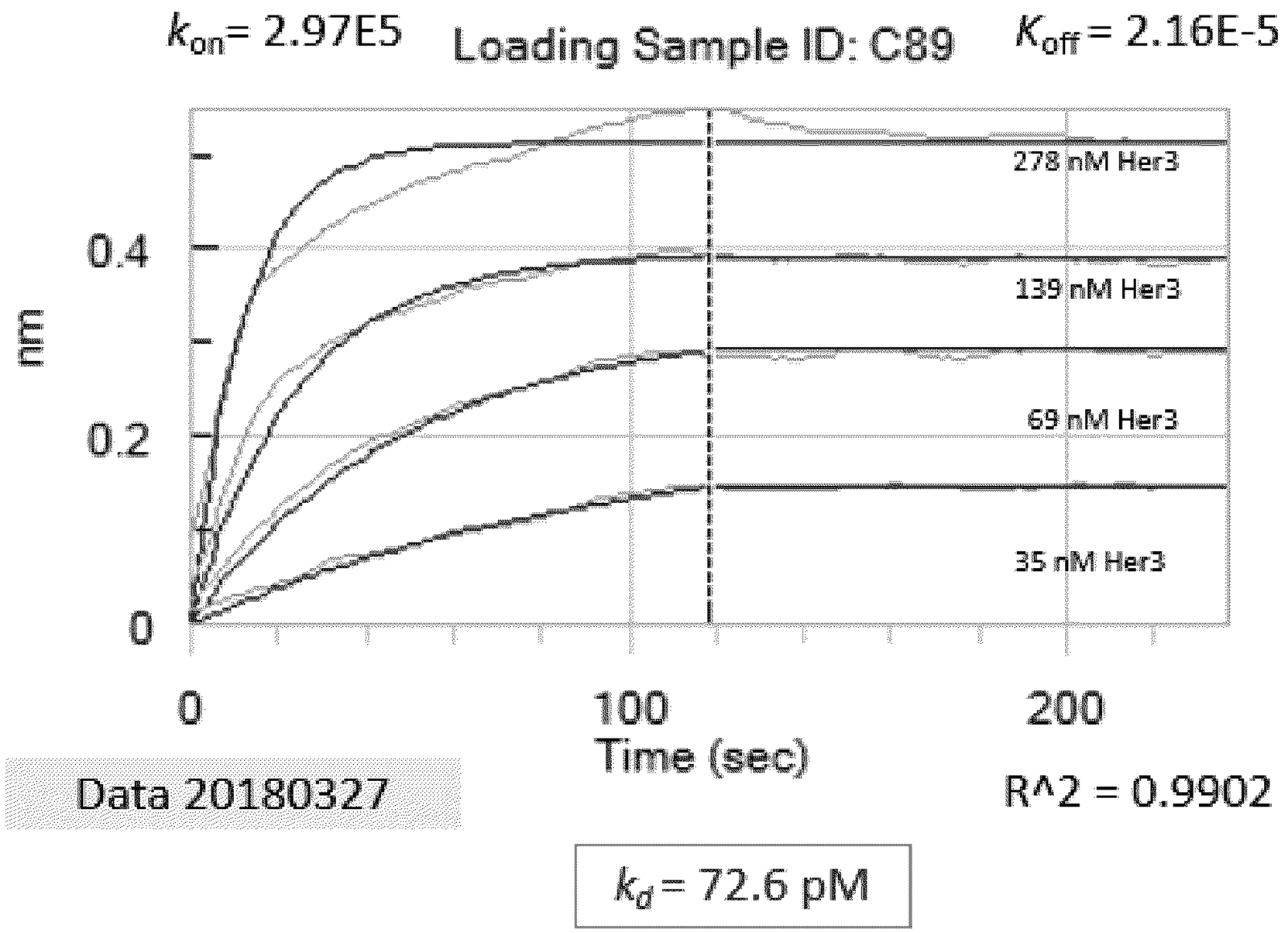
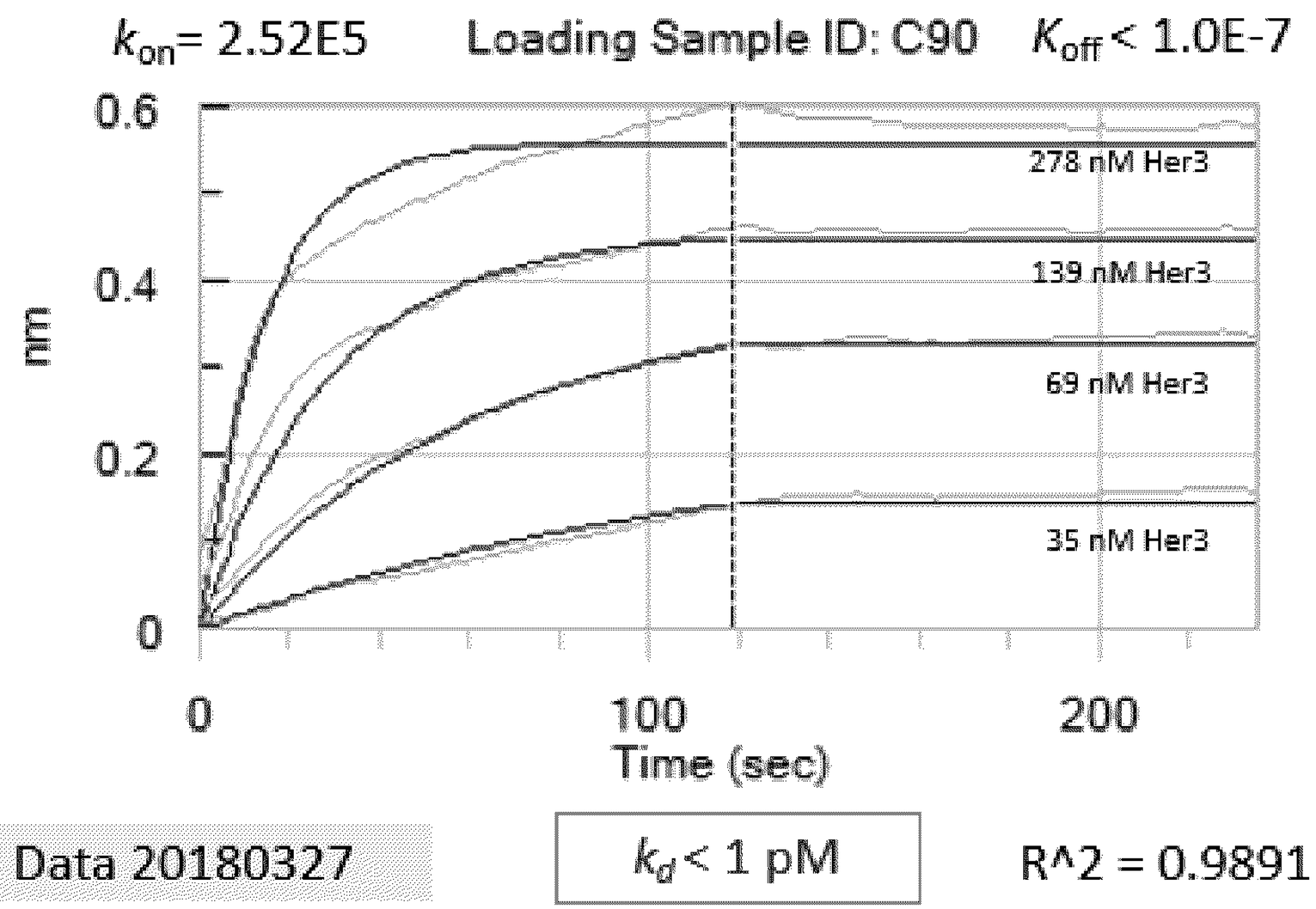


Figure 35C



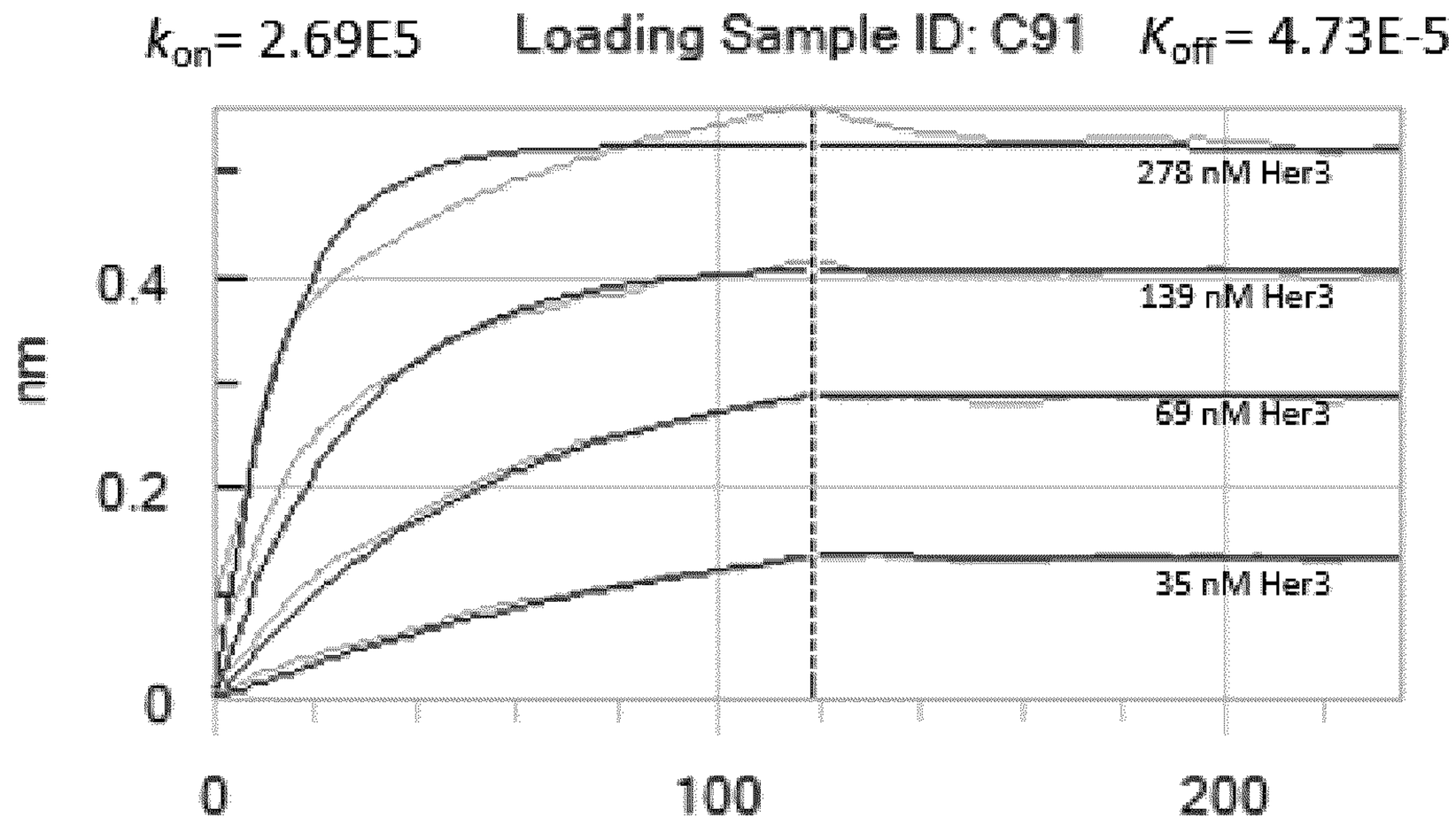
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C89	2	69	0.2882	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.3206	0.0063	2.05E-02	0.3202	99.9	0.0341	0.9902
C89	2	35	0.1471	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.2068	0.0071	1.04E-02	0.2064	99.8	0.0341	0.9902
C89	2	278	0.5458	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.513	0.0041	8.26E-02	0.5129	100	0.0341	0.9902
C89	2	139	0.3968	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.3943	0.0046	4.13E-02	0.3941	99.9	0.0341	0.9902

Figure 36A



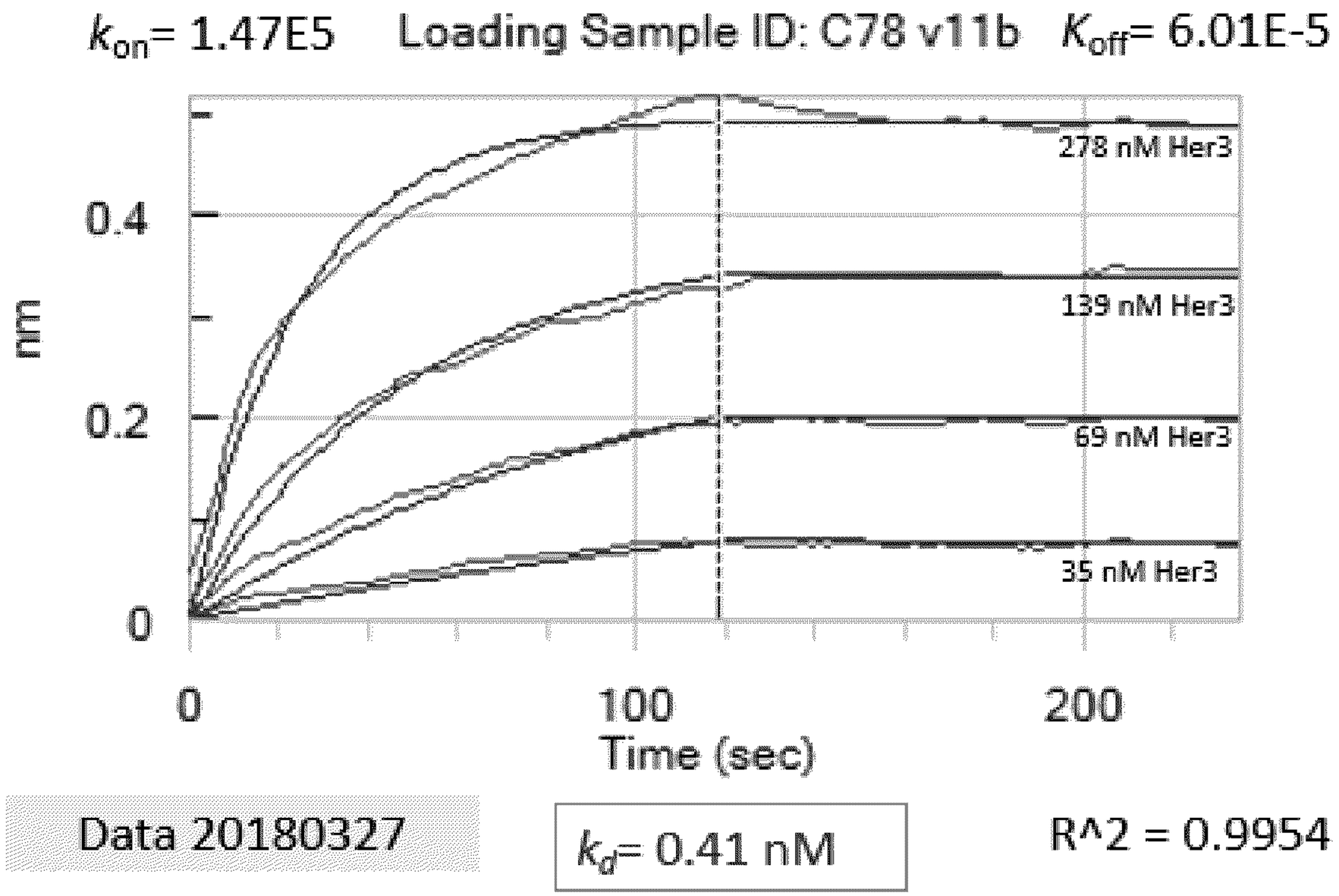
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C90	6	35	0.1355	<1.0E-12	5.13E-10	2.52E+05	1.04E+04	<1.0E-07		0.2209	0.0092	8.80E-03	0.2209	100	0.0457	0.9891
C90	6	278	0.5944	<1.0E-12	5.13E-10	2.52E+05	1.04E+04	<1.0E-07		0.5578	0.0053	6.99E-02	0.5578	100	0.0457	0.9891
C90	6	139	0.4533	<1.0E-12	5.13E-10	2.52E+05	1.04E+04	<1.0E-07		0.4543	0.0064	3.50E-02	0.4543	100	0.0457	0.9891
C90	6	69	0.3221	<1.0E-12	5.13E-10	2.52E+05	1.04E+04	<1.0E-07		0.3709	0.009	1.74E-02	0.3709	100	0.0457	0.9891

Figure 36B



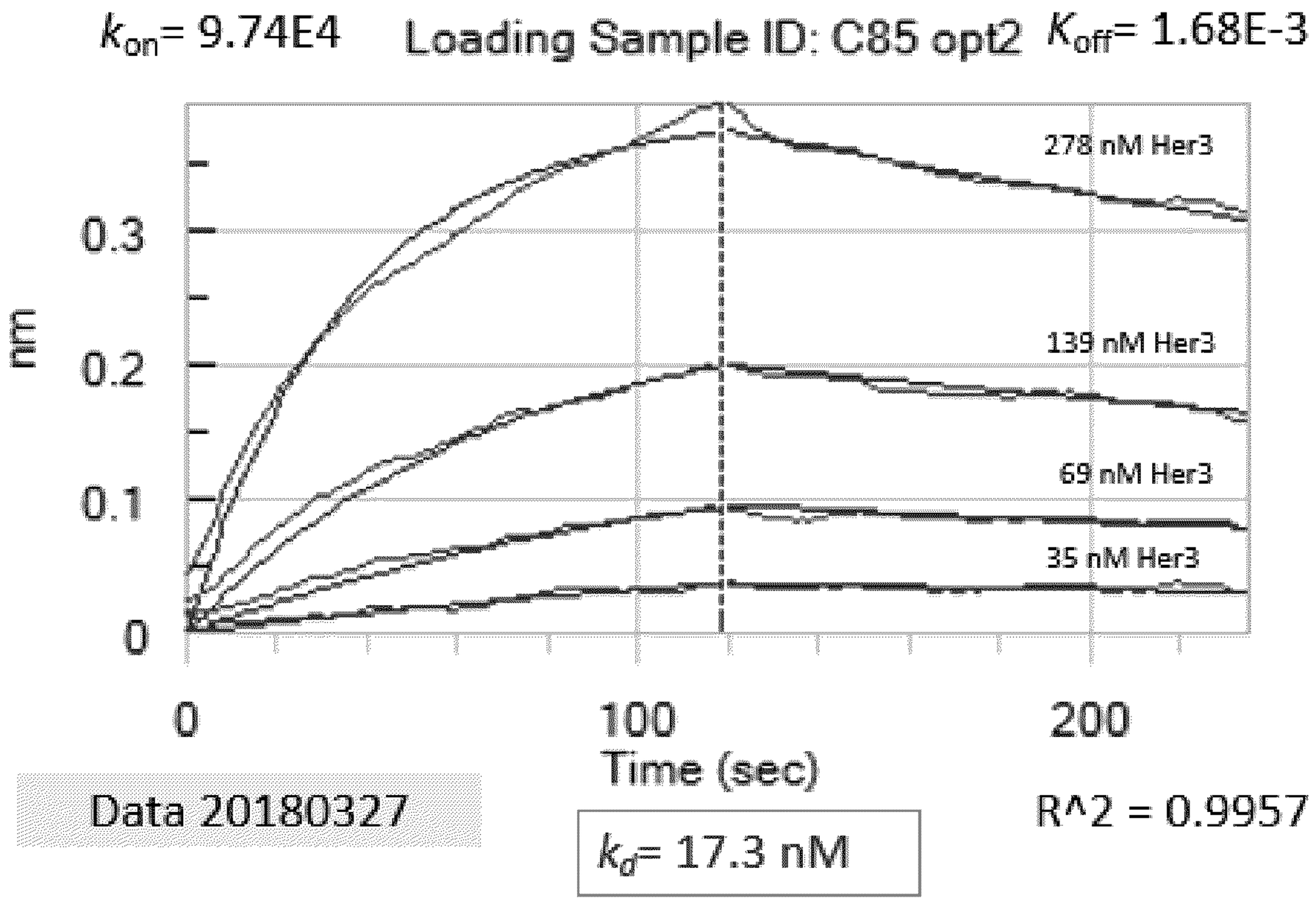
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C91	3	35	0.1286	1.76E-10	4.12E-10	2.69E+05	9.57E+03	4.73E-05	1.11E-04	0.202	0.0071	9.46E-03	0.201	99.5	0.033	0.9917
C91	3	139	0.4098	1.76E-10	4.12E-10	2.69E+05	9.57E+03	4.73E-05	1.11E-04	0.4132	0.0048	3.74E-02	0.4127	99.9	0.033	0.9917
C91	3	278	0.5575	1.76E-10	4.12E-10	2.69E+05	9.57E+03	4.73E-05	1.11E-04	0.5255	0.0041	7.48E-02	0.5252	99.9	0.033	0.9917
C91	3	69	0.2851	1.76E-10	4.12E-10	2.69E+05	9.57E+03	4.73E-05	1.11E-04	0.3242	0.0065	1.86E-02	0.3234	99.7	0.033	0.9917

Figure 36C



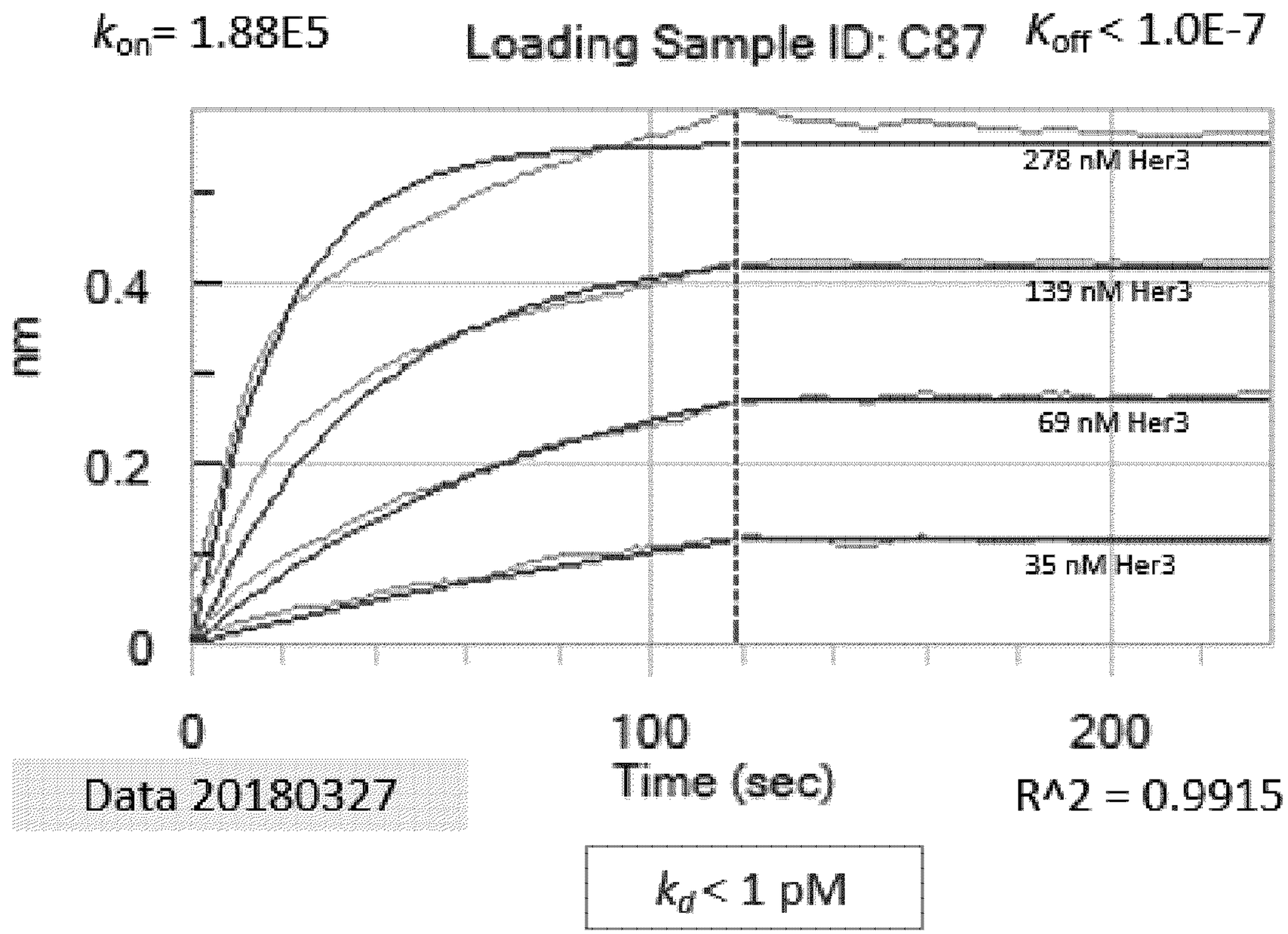
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C78 v11b	7	69	0.1929	4.10E-10	6.84E-10	1.47E+05	4.57E+03	6.01E-05	1.00E-04	0.288	0.0074	1.02E-02	0.2863	99.4	0.0157	0.9954
C78 v11b	7	35	0.0786	4.10E-10	6.84E-10	1.47E+05	4.57E+03	6.01E-05	1.00E-04	0.1714	0.0072	5.19E-03	0.1695	98.8	0.0157	0.9954
C78 v11b	7	139	0.3283	4.10E-10	6.84E-10	1.47E+05	4.57E+03	6.01E-05	1.00E-04	0.3745	0.006	2.04E-02	0.3734	99.7	0.0157	0.9954
C78 v11b	7	278	0.5147	4.10E-10	6.84E-10	1.47E+05	4.57E+03	6.01E-05	1.00E-04	0.4982	0.0045	4.08E-02	0.4975	99.9	0.0157	0.9954

Figure 36D



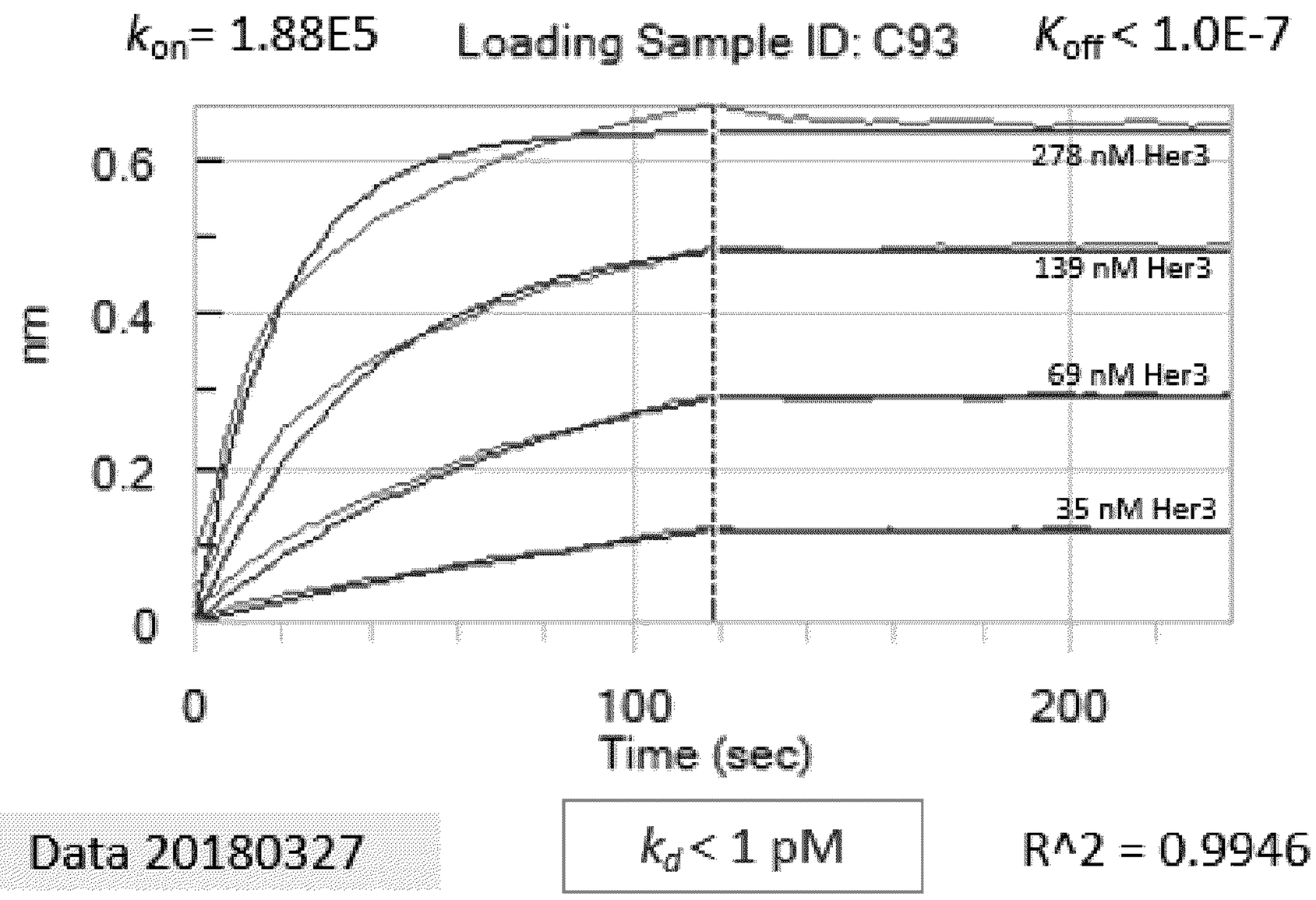
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C85 opt2	5	139	0.1967	1.73E-08	1.35E-09	9.74E+04	3.54E+03	1.68E-03	1.16E-04	0.2686	0.0066	1.52E-02	0.2389	88.9	0.0086	0.9957
C85 opt2	5	35	0.0338	1.73E-08	1.35E-09	9.74E+04	3.54E+03	1.68E-03	1.16E-04	0.1225	0.0074	5.09E-03	0.082	66.9	0.0086	0.9957
C85 opt2	5	278	0.3885	1.73E-08	1.35E-09	9.74E+04	3.54E+03	1.68E-03	1.16E-04	0.4109	0.006	2.88E-02	0.3868	94.1	0.0086	0.9957
C85 opt2	5	69	0.0911	1.73E-08	1.35E-09	9.74E+04	3.54E+03	1.68E-03	1.16E-04	0.1881	0.0069	8.40E-03	0.1504	80	0.0086	0.9957

Figure 36E



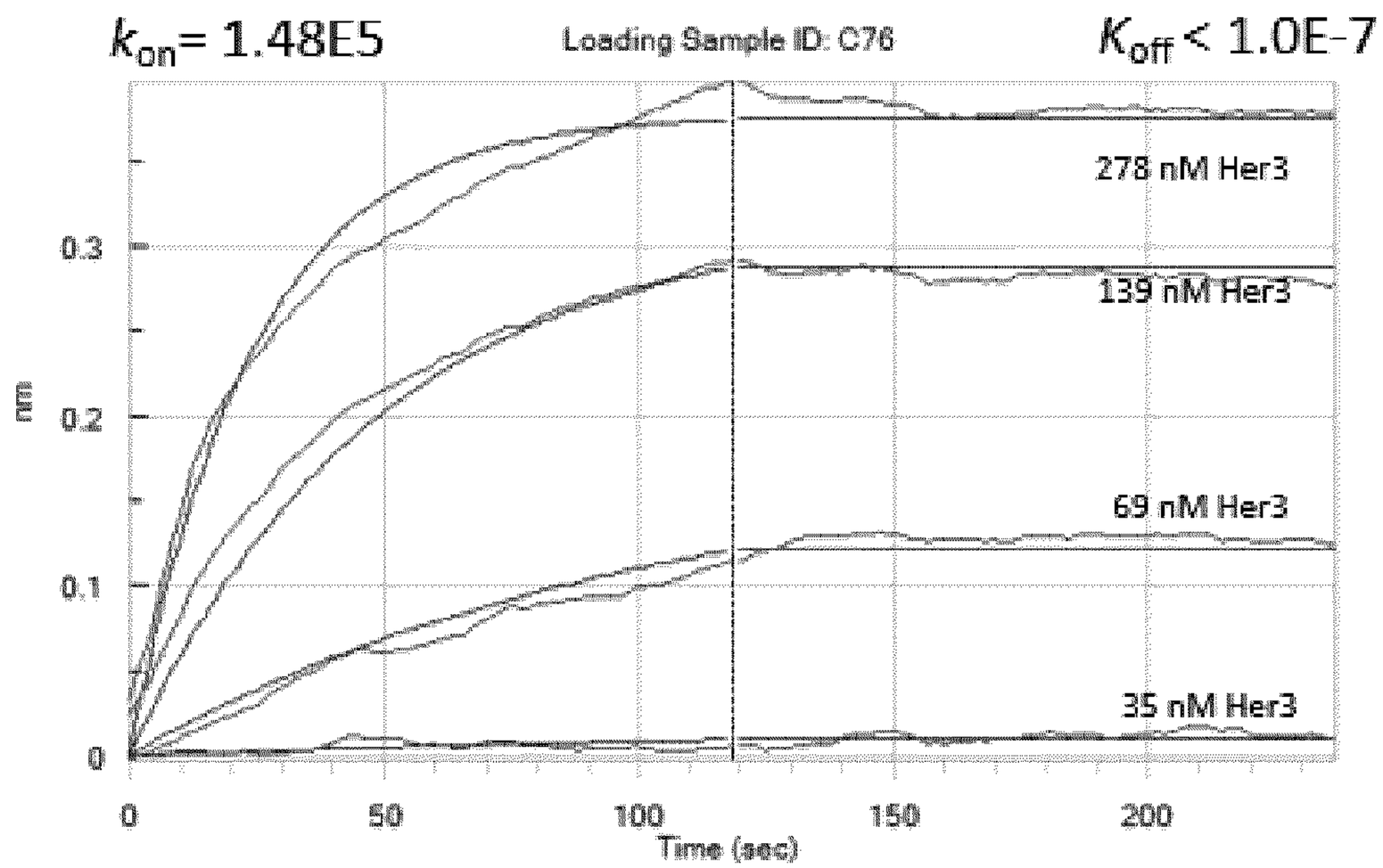
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C87	4	278	0.5768	<1.0E-12	6.64E-10	1.88E+05	7.36E+03	<1.0E-07		0.5516	0.0055	5.23E-02	0.5516	100	0.0357	0.9915
C87	4	69	0.2569	<1.0E-12	6.64E-10	1.88E+05	7.36E+03	<1.0E-07		0.3401	0.0095	1.30E-02	0.3401	100	0.0357	0.9915
C87	4	139	0.4134	<1.0E-12	6.64E-10	1.88E+05	7.36E+03	<1.0E-07		0.4359	0.0072	2.62E-02	0.4359	100	0.0357	0.9915
C87	4	35	0.114	<1.0E-12	6.64E-10	1.88E+05	7.36E+03	<1.0E-07		0.2098	0.0096	6.59E-03	0.2098	100	0.0357	0.9915

Figure 36F



Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C93	1	69	0.2877	<1.0E-12	5.46E-10	1.88E+05	5.99E+03	<1.0E-07		0.37	0.0086	1.30E-02	0.37	100	0.0335	0.9946
C93	1	278	0.6639	<1.0E-12	5.46E-10	1.88E+05	5.99E+03	<1.0E-07		0.6372	0.0052	5.22E-02	0.6372	100	0.0335	0.9946
C93	1	139	0.4777	<1.0E-12	5.46E-10	1.88E+05	5.99E+03	<1.0E-07		0.5032	0.0068	2.61E-02	0.5032	100	0.0335	0.9946
C93	1	35	0.119	<1.0E-12	5.46E-10	1.88E+05	5.99E+03	<1.0E-07		0.2179	0.0086	6.58E-03	0.2179	100	0.0335	0.9946

Figure 36G



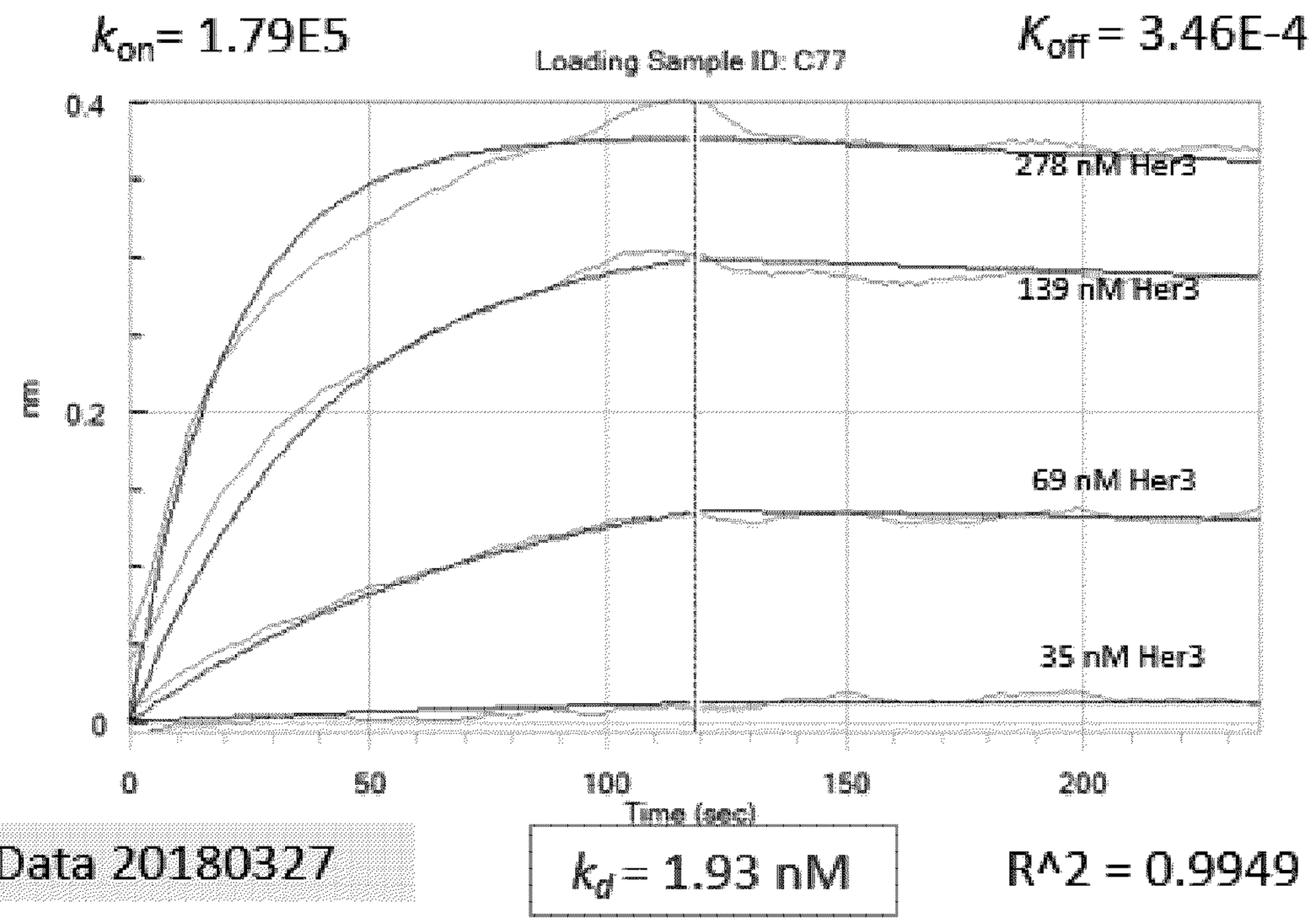
Data 20180327

k_d < 1 pM

R^2 = 0.9951

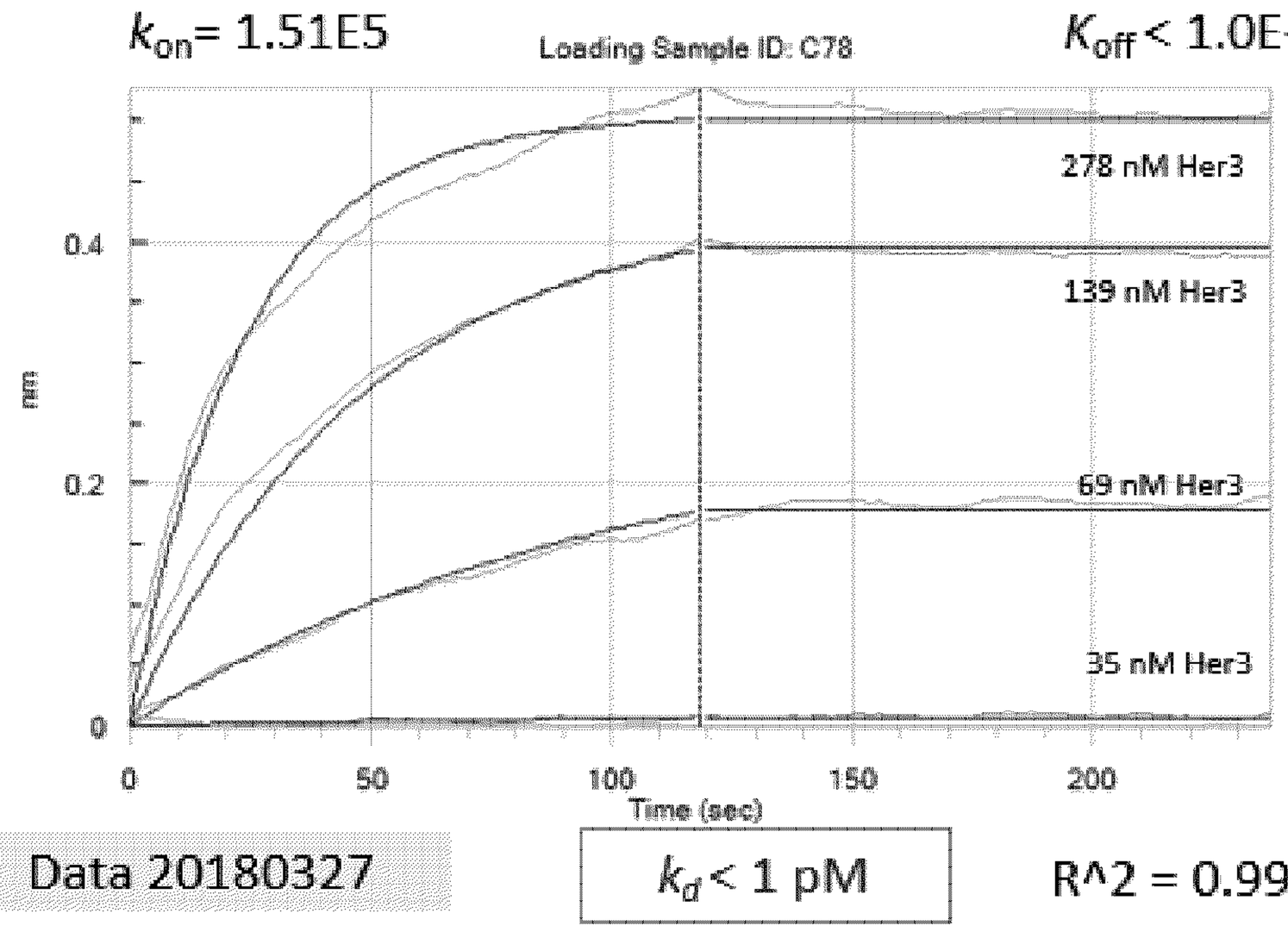
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C76	3	278	0.3903	<1.0E-12	7.94E-10	1.48E+05	5.36E+03	<1.0E-07		0.3772	0.004	4.13E-02	0.3772	100	0.0122	0.9951
C76	3	139	0.2888	<1.0E-12	7.94E-10	1.48E+05	5.36E+03	<1.0E-07		0.3143	0.0057	2.06E-02	0.3143	100	0.0122	0.9951
C76	3	69	0.1082	<1.0E-12	7.94E-10	1.48E+05	5.36E+03	<1.0E-07		0.172	0.0054	1.02E-02	0.172	100	0.0122	0.9951
C76	3	35	0.0037	<1.0E-12	7.94E-10	1.48E+05	5.36E+03	<1.0E-07		0.0208	0.0047	5.19E-03	0.0208	100	0.0122	0.9951

Figure 36H



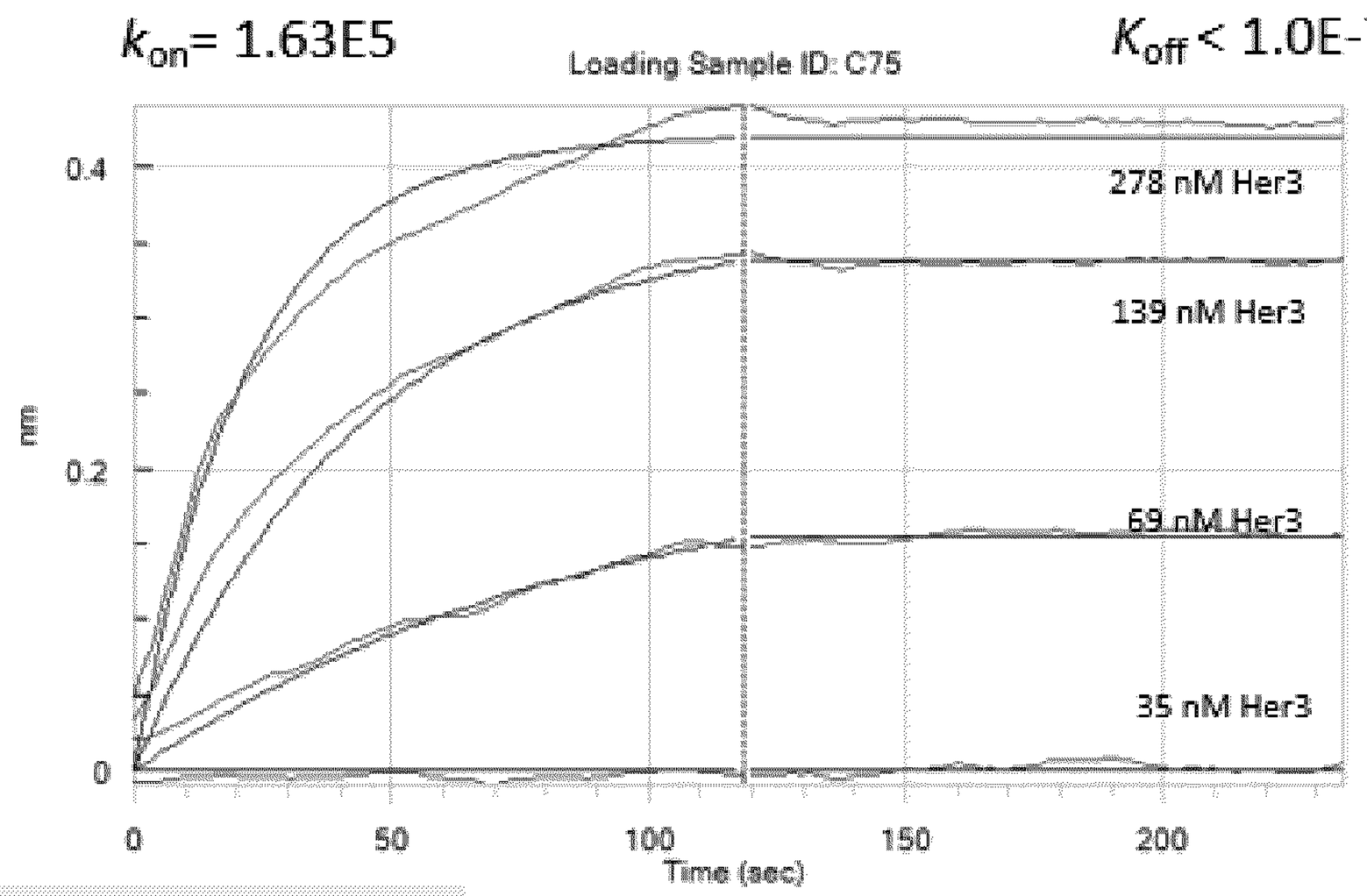
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C77	2	35	0.0096	1.93E-09	6.58E-10	1.79E+05	6.34E+03	3.46E-04	1.17E-04	0.0236	0.0043	6.62E-03	0.0224	94.8	0.0142	0.9949
C77	2	69	0.1318	1.93E-09	6.58E-10	1.79E+05	6.34E+03	3.46E-04	1.17E-04	0.1704	0.0051	1.27E-02	0.1745	97.3	0.0142	0.9949
C77	2	139	0.3036	1.93E-09	6.58E-10	1.79E+05	6.34E+03	3.46E-04	1.17E-04	0.3187	0.005	2.53E-02	0.3143	98.6	0.0142	0.9949
C77	2	278	0.3985	1.93E-09	6.58E-10	1.79E+05	6.34E+03	3.46E-04	1.17E-04	0.3804	0.0038	5.02E-02	0.3778	99.3	0.0142	0.9949

Figure 36I



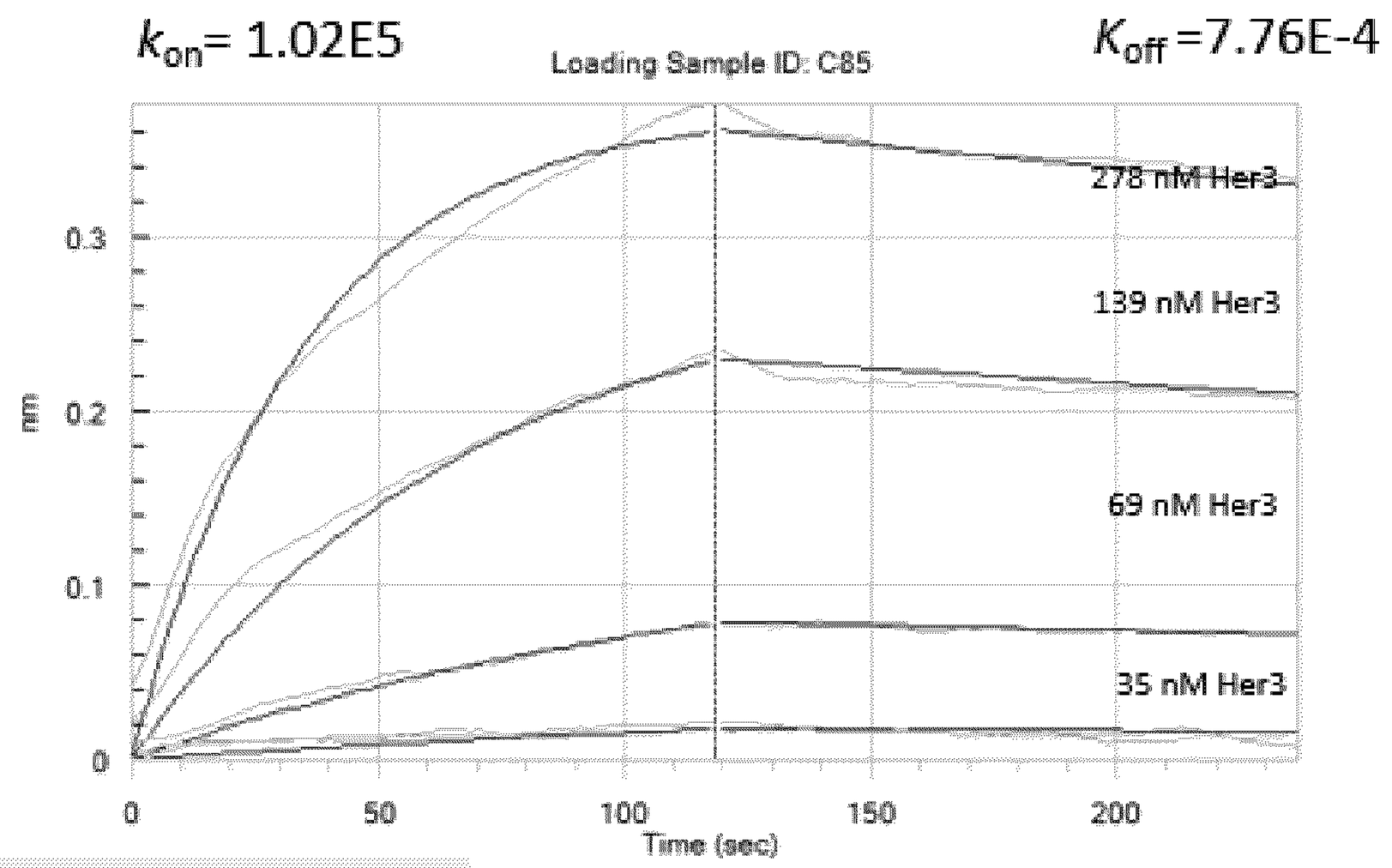
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C78	4	278	0.5153	<1.0E-12	6.54E-10	1.51E+05	4.60E+03	<1.0E-07		0.5037	0.0044	4.21E-02	0.5037	100	0.0176	0.9965
C78	4	35	0.0036	<1.0E-12	6.54E-10	1.51E+05	4.60E+03	<1.0E-07		0.0138	0.0052	5.30E-03	0.0138	100	0.0176	0.9965
C78	4	69	0.1598	<1.0E-12	6.54E-10	1.51E+05	4.60E+03	<1.0E-07		0.2495	0.0064	1.04E-02	0.2495	100	0.0176	0.9965
C78	4	139	0.3891	<1.0E-12	6.54E-10	1.51E+05	4.60E+03	<1.0E-07		0.429	0.0064	2.10E-02	0.429	100	0.0176	0.9965

Figure 36J



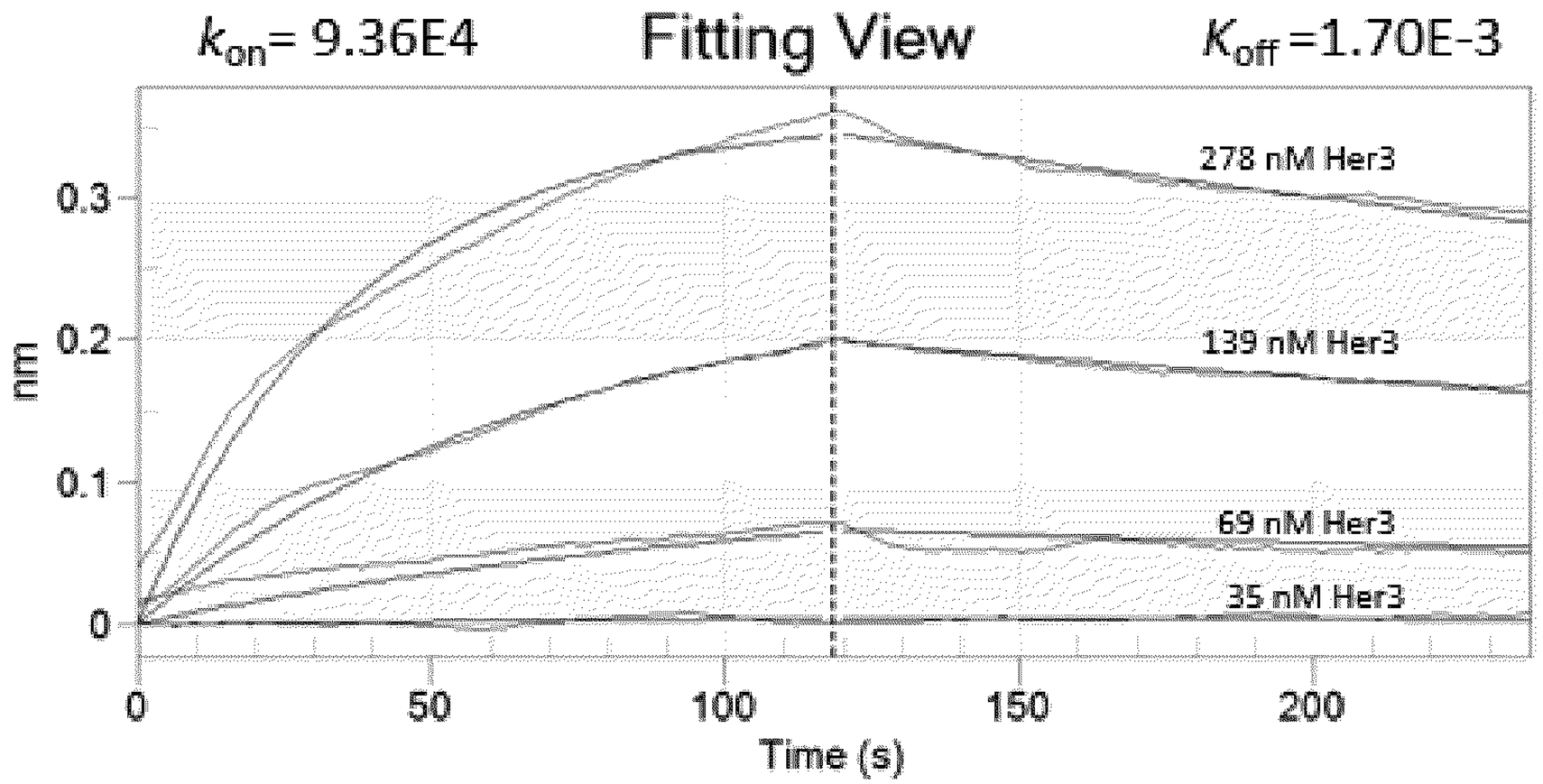
Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C75	5	69	0.1507	<1.0E-12	6.91E-10	1.63E+05	5.62E+03	<1.0E-07		0.2092	0.0059	1.12E-02	0.2092	100	0.0161	0.9955
C75	5	139	0.3396	<1.0E-12	6.91E-10	1.63E+05	5.62E+03	<1.0E-07		0.3632	0.0059	2.27E-02	0.3632	100	0.0161	0.9955
C75	5	278	0.4384	<1.0E-12	6.91E-10	1.63E+05	5.62E+03	<1.0E-07		0.4216	0.004	4.53E-02	0.4216	100	0.0161	0.9955
C75	5	35	-0.0012	<1.0E-12	6.91E-10	1.63E+05	5.62E+03	<1.0E-07		0		5.70E-03	0	100	0.0161	0.9955

Figure 36K



Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C85	1	278	0.3712	7.58E-09	1.19E-09	1.02E+05	3.85E+03	7.76E-04	1.19E-04	0.3816	0.0054	2.92E-02	0.3715	97.3	0.0091	0.9957
C85	1	69	0.0753	7.58E-09	1.19E-09	1.02E+05	3.85E+03	7.76E-04	1.19E-04	0.1436	0.0057	7.83E-03	0.1294	90.1	0.0091	0.9957
C85	1	139	0.2284	7.58E-09	1.19E-09	1.02E+05	3.85E+03	7.76E-04	1.19E-04	0.2898	0.007	1.50E-02	0.2748	94.8	0.0091	0.9957
C85	1	35	0.017	7.58E-09	1.19E-09	1.02E+05	3.85E+03	7.76E-04	1.19E-04	0.053	0.0059	4.36E-03	0.0435	82.2	0.0091	0.9957

Figure 36L



Data 20180327

k_d = 18.2 nM

R^2 = 0.9957

Loading Sample ID	Cycle	Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
C85 opt1	1	278	0.3524	1.82E-08	1.54E-09	9.36E+04	3.75E+03	1.70E-03	1.27E-04	0.3807	0.0063	2.77E-02	0.3573	93.9	0.008	0.9957
C85 opt1	1	139	0.1929	1.82E-08	1.54E-09	9.36E+04	3.75E+03	1.70E-03	1.27E-04	0.2709	0.0074	1.47E-02	0.2396	88.4	0.008	0.9957
C85 opt1	1	69	0.0697	1.82E-08	1.54E-09	9.36E+04	3.75E+03	1.70E-03	1.27E-04	0.1329	0.0059	8.16E-03	0.1052	79.2	0.008	0.9957
C85 opt1	1	35	0.0006	1.82E-08	1.54E-09	9.36E+04	3.75E+03	1.70E-03	1.27E-04	0.0131	0.0061	4.97E-03	0.0088	65.8	0.008	0.9957

Figure 36M

Clones	Heavy Chain	Light Chain	Developability								
	Homology	Homology	Deamidation (NS, NG, NH, NN)	Isomerization (DS, DG)	Protease Cleavage (DP)	Free Cys	Exposed M	Glycosylation	Immunogenicity (HC+LC)	pI_HC	pI_LC
10D1_c75	82.5%(Hu)	80.0%(Ma)	NG,	None	None	None	YES (CDR3)	NPT	3+6	8.102	6.615
10D1_c76	83.5%(Hu)	77.9%(Ma)	NG,	None	None	None	YES (CDR3)	NPS	3+5	8.121	6.614
10D1_c77	83.5%(Hu)	78.5%(Hu)	NG,	None	None	None	YES (CDR3)	NPS	4+3	8.121	7.618
10D1_c78	83.5%(Hu)	81.1%(Ma)	None	None	None	None	YES (CDR3)	NPS	3+3	8.591	8.128
V11b78L	88.7%(Hu)	81.1%(Ma)	None	None	None	None	YES (CDR3)	NPS	3+3	8.453	8.128
10D1_c85	82.5% (Hu)	81.1%(Ma)	None	None	None	None	YES (CDR3)	NPS	1+3	8.952	8.578
10D1_c85_opt1	83.5% (Hu)	81.1%(Ma)	None	None	None	None	NO	NPS	0+3	8.6	8.578
10D1_c85_opt2	83.5% (Hu)	81.1%(Ma)	None	None	None	None	NO	NPS	0+3	8.952	8.578
10D1_c87	82.5% (Hu)	80.0%(Ma)	NG,	None	None	None	YES (CDR3)	NPS	3+5	8.13	4.646
10D1_c89	89.9% (Hu)	85.3% (Hu/Ma)	None	None	None	None	YES (CDR3)	None	3+4	7.965	6.545
10D1_c90	89.9% (Hu)	80.0% (Ma)	None	None	None	None	YES (CDR3)	None	3+4	7.965	5.388
10D1_c91	87.9% (Hu)	84.2 (Hu/Ma)	None	None	None	None	YES (CDR3)	None	3+3	7.935	7.468
10D1_c92	82.5% (Hu)	78.9% (Ma)	None	None	None	None	YES (CDR3)	N.A.	4+6	8.07	6.46
10D1_c93	82.5% (Hu)	82.1%(Ma)	NG	None	None	None	YES (CDR3)	NPS	3+5	8.13	7.535

Figure 37

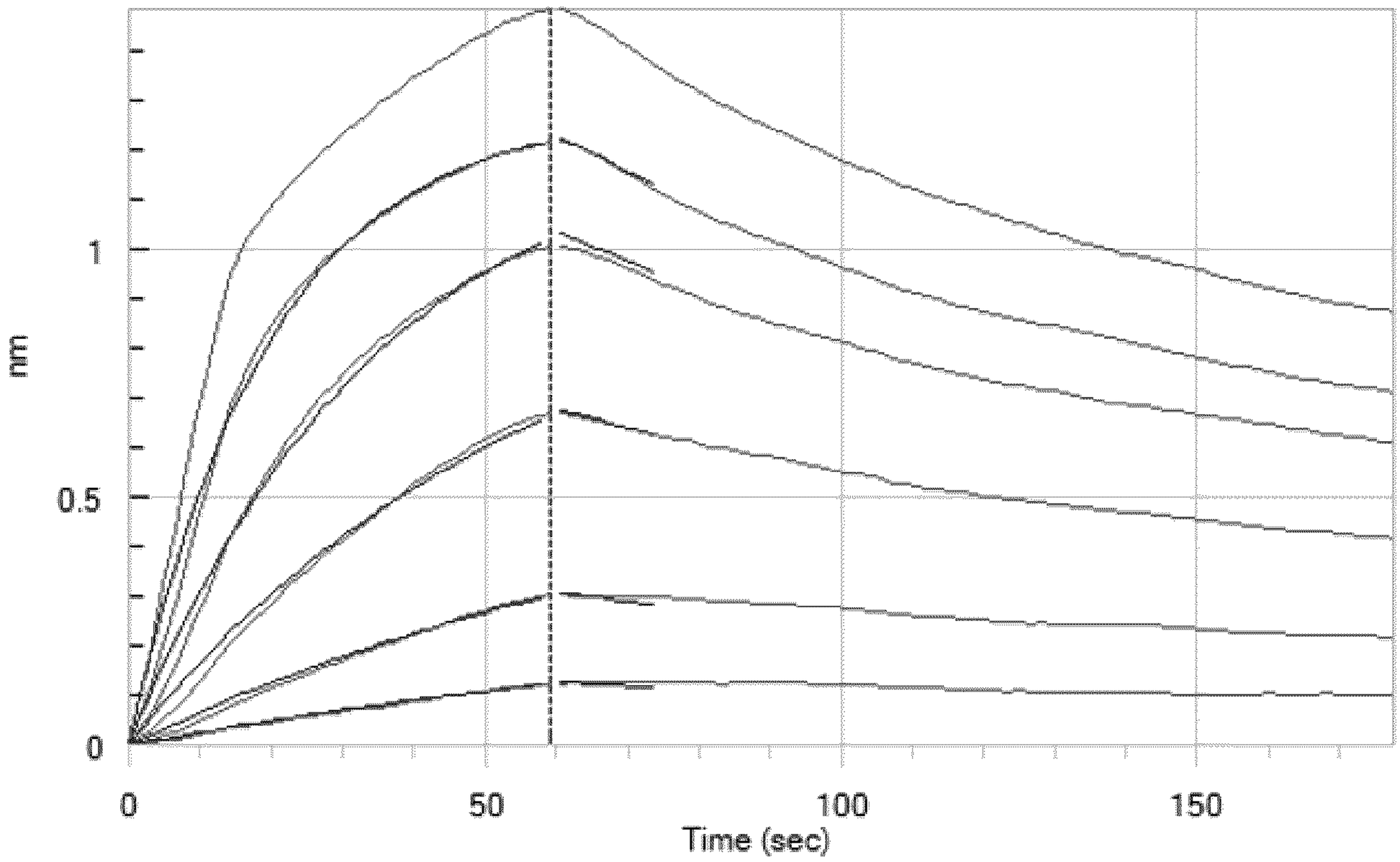


Figure 38A

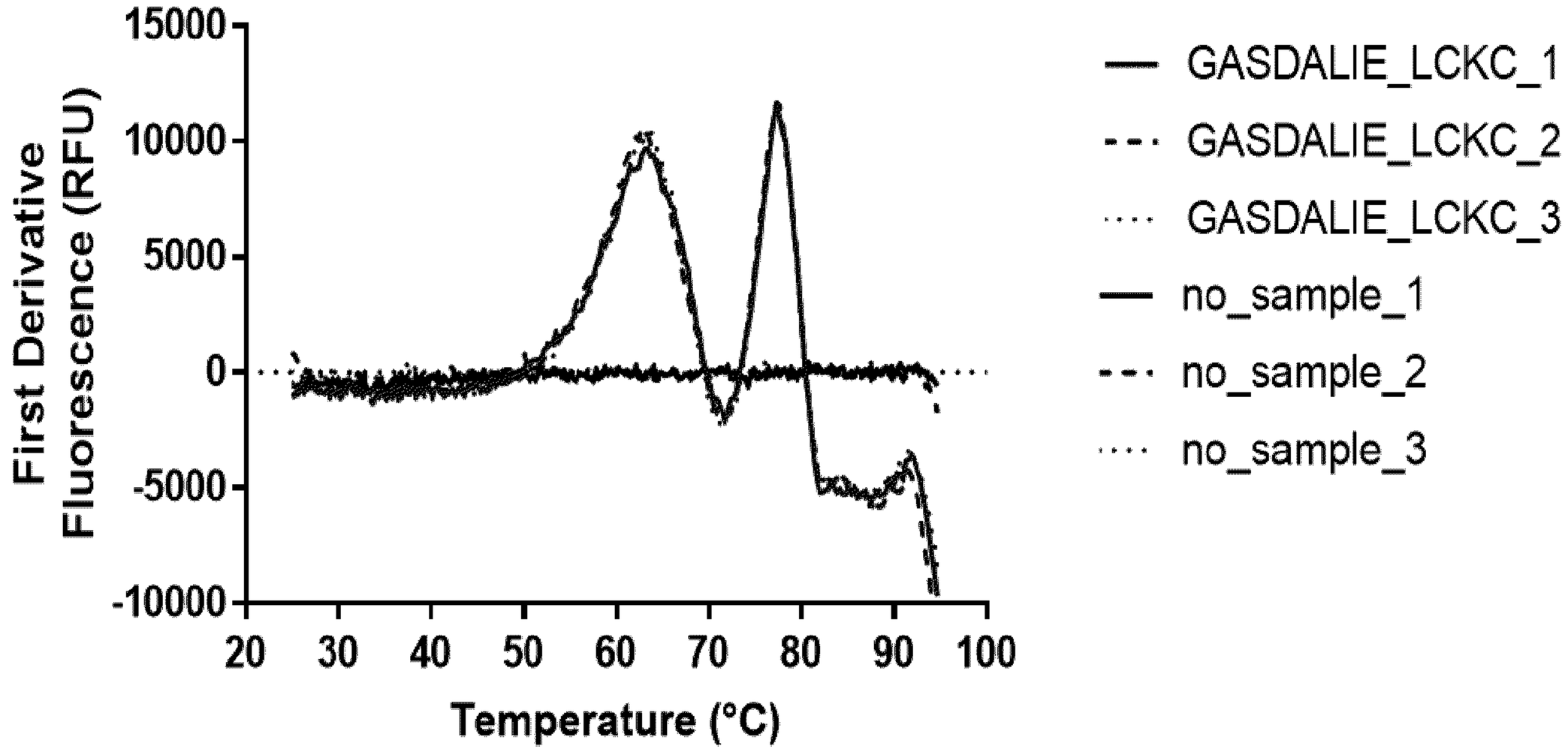


Figure 38B

$K_{on} = 1.3e^5\ M^{-1}\ s^{-1}$ $K_d = 298\ nM$ $K_{dis} = 4.0e^{-2}\ s^{-1}$

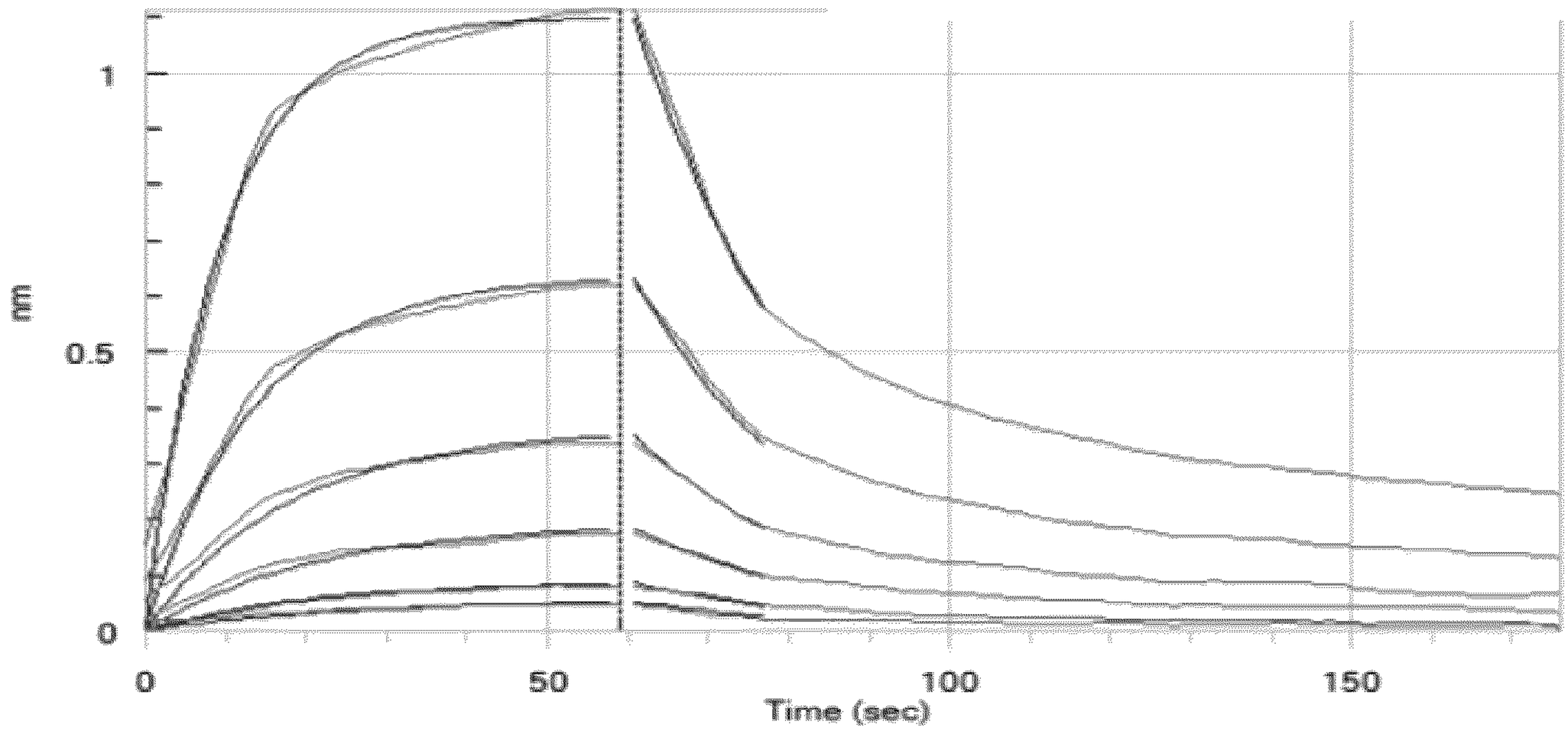


Figure 39A

$K_{on} = 1.6e^5\ M^{-1}\ s^{-1}$ $K_d = 58\ nM$ $K_{dis} = 0.90e^{-2}\ s^{-1}$

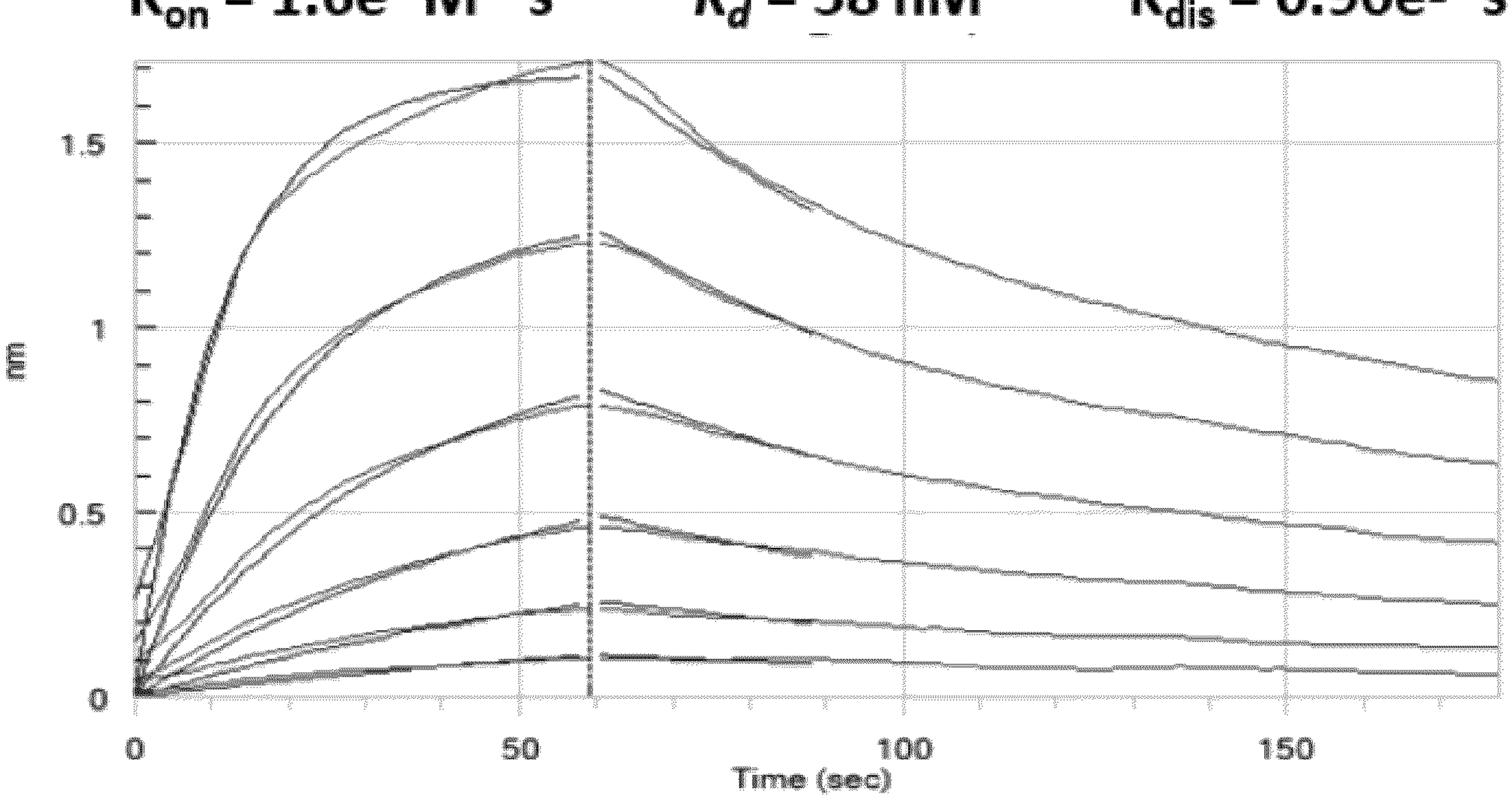


Figure 39B

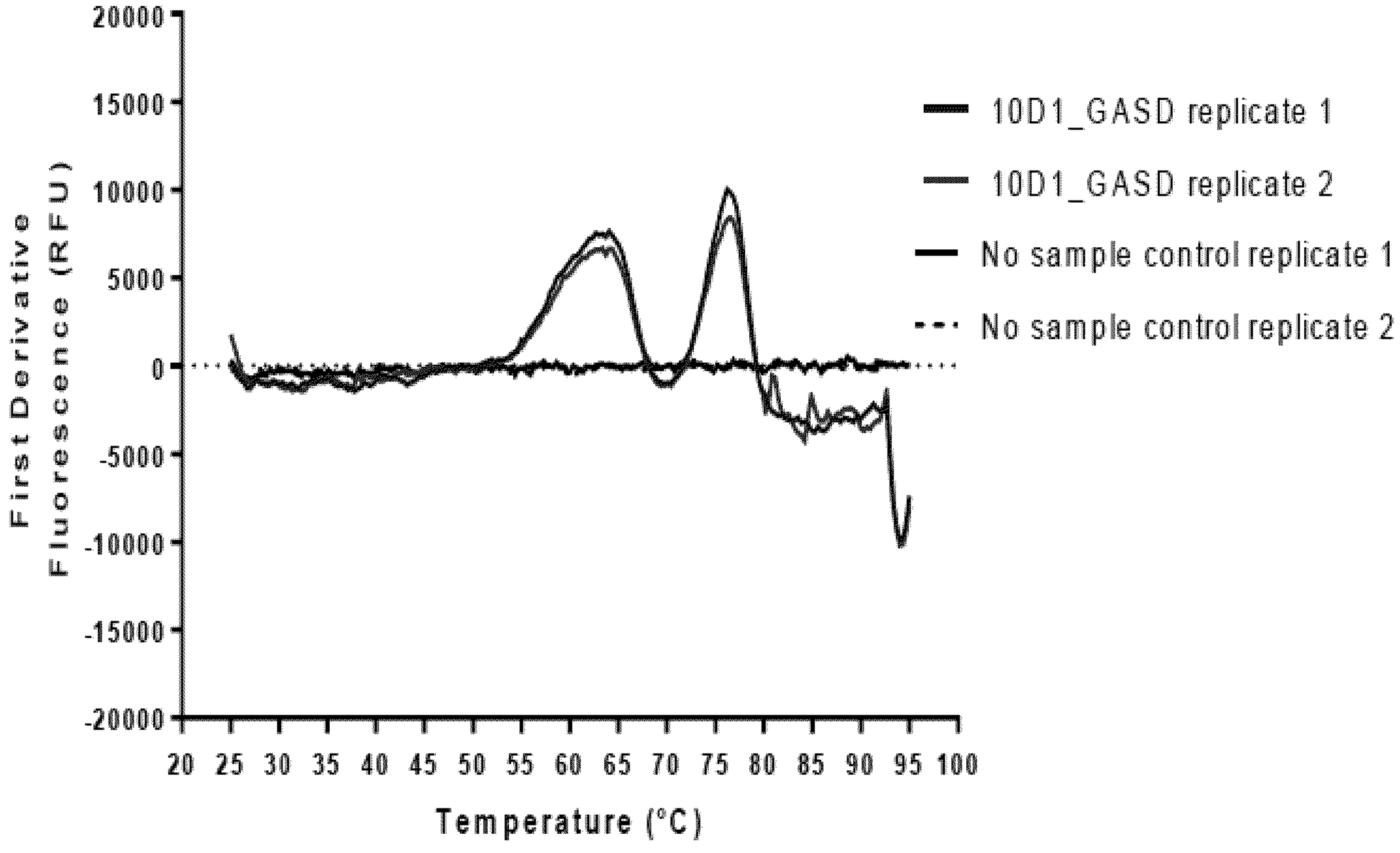

20000
15000
10000
5000
0
-5000
-10000
-15000
-20000
First Derivative Fluorescence (RFU)
20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100
Temperature (°C)
10D1_GASD replicate 1
10D1_GASD replicate 2
No sample control replicate 1
No sample control replicate 2

Figure 40

Receptor	Gene	Function	Binding Affinity	Reported K_D (nM)	10D1F.FcA: 10D1F hIgG1 K_D (nM)	10D1F.FcB: 10D1F hIgG1 GASDALIE-LCKC K_D (nM)	10D1F hIgG1 N297Q K_D (nM)	10D1F hIgG2 K_D (nM)	10D1F hIgG4 K_D (nM)	UM716 hIgG1 K_D (nM)	Seribantumab hIgG2 K_D (nM)
FcRn	FCGRT	Recycling (Increased affinity → Increased half life)	Medium	hIgG1: 737 hIgG2: 540 hIgG3: 585 hIgG4: 717	47.6	37.4	54.6	6.43	10.3	16.5	11.5
FcgRIIIA (V158)	CD16A	Cell activation	Medium	hIgG1: 252-500 hIgG2: 14286 hIgG3: 102 hIgG4: 4000	986	82.1	ND	ND	ND	705	7050
FcgRIIIA (F158)	CD16A	Cell activation	Low	hIgG1: 855-4454 hIgG2: 33333 hIgG3: 130 hIgG4: 5000	ND	162	ND	ND	ND	5380	ND
FcgRIIA (H167)	CD32A	Cell activation	Low	hIgG1: 192-4486 hIgG2: 2222 hIgG3: 1124 hIgG4: 5882	1800	561	ND	670	ND	1480	222
FcgRIIA (R167)	CD32A	Cell activation	Low	hIgG1: 286-1550 hIgG2: 10000 hIgG3: 1099 hIgG4: 4762	976	400	ND	ND	ND	1500	243
FcgRIIB	CD32B	Cell inhibition	Low	hIgG1: 500-9275 hIgG2: 50000 hIgG3: 5882 hIgG4: 5000	ND	580	ND	ND	ND	ND	1440

Figure 41A

Receptor	Gene	Function	Binding affinity	Reported K_D (nM)		10D1F.FcA 10D1F hIgG1 K_D (nM)	10D1F.FcB 10D1F hIgG1 GASDALIE-LCKC K_D (nM)	10D1F hIgG1 N297Q K_D (nM)	10D1F hIgG2 K_D (nM)	10D1F hIgG4 K_D (nM)	LJM716 hIgG1 K_D (nM)	Seribantumab hIgG2 K_D (nM)
moFcRn	FCGRT	Recycling (Increased affinity → Increased half life)	Medium	mIgG1: 1157 mIgG2a: 490 mIgG2b: 545 mIgG3: 140	hIgG1: 72 hIgG2: 63 hIgG3: 230 hIgG4: 116	14.6	15.2	13.7	7.33	13	12.8	6.69
moFcgRIV	CD16-2	Cell activation	High	mIgG1: ND mIgG2a: 34.5 mIgG2b: 59 mIgG3: ND	hIgG1: 280 hIgG2: ND hIgG3: 170 hIgG4: 26000	1,810	55.4	ND	ND	ND	701	ND
moFcgRIII	CD16	Cell activation	Low	mIgG1: 3200 mIgG2a: 1460 mIgG2b: 1555 mIgG3: ND	hIgG1: 9300 hIgG2: 9700 hIgG3: 1300 hIgG4: 21000	ND	ND	ND	ND	ND	ND	ND
moFcgRIIb	CD32	Cell inhibition	Low	mIgG1: 301 mIgG2a: 2390 mIgG2b: 448 mIgG3: ND	hIgG1: 1100 hIgG2: 7900 hIgG3: 700 hIgG4: 11000	ND	ND	ND	ND	ND	ND	ND

Figure 41B

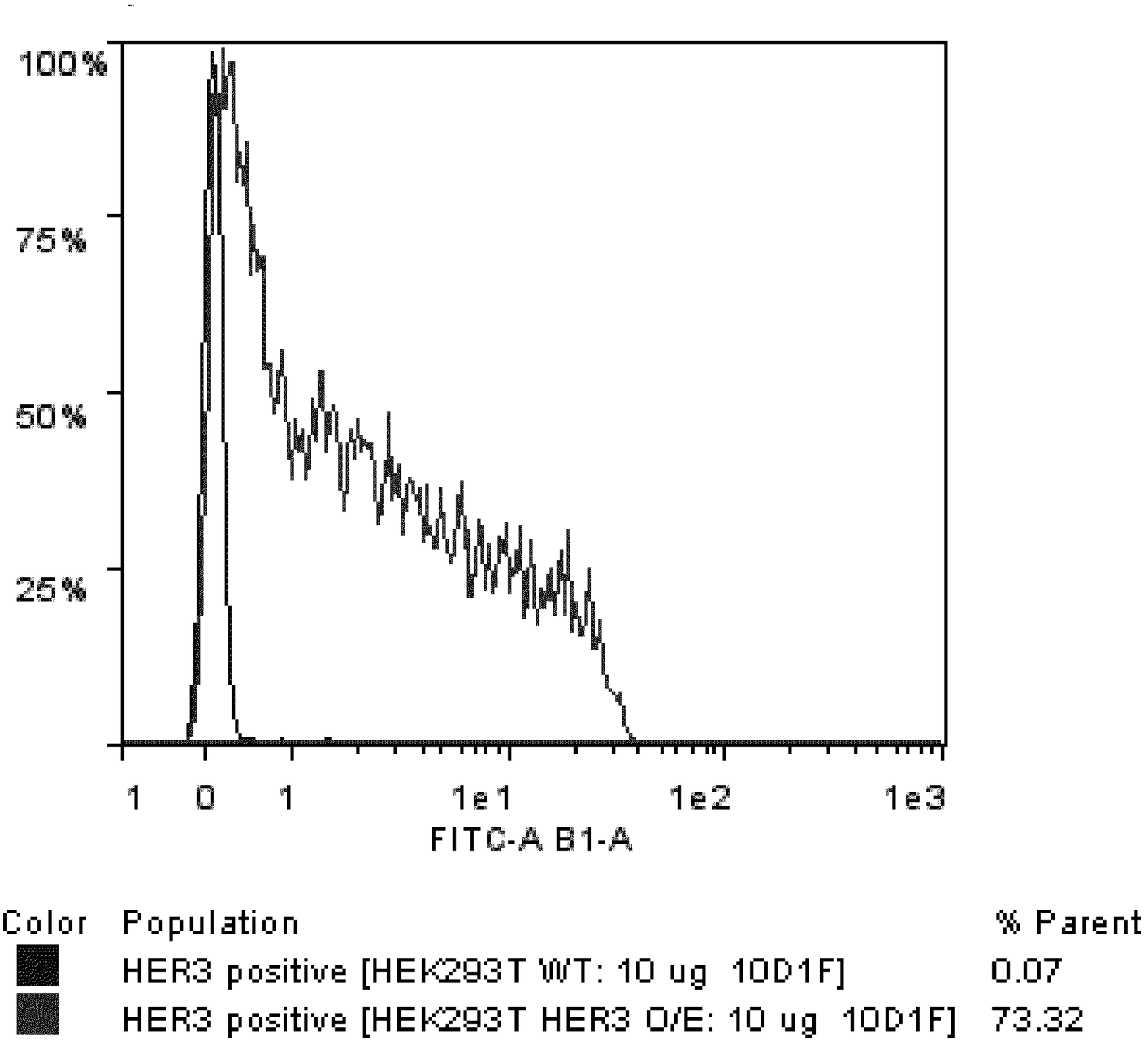
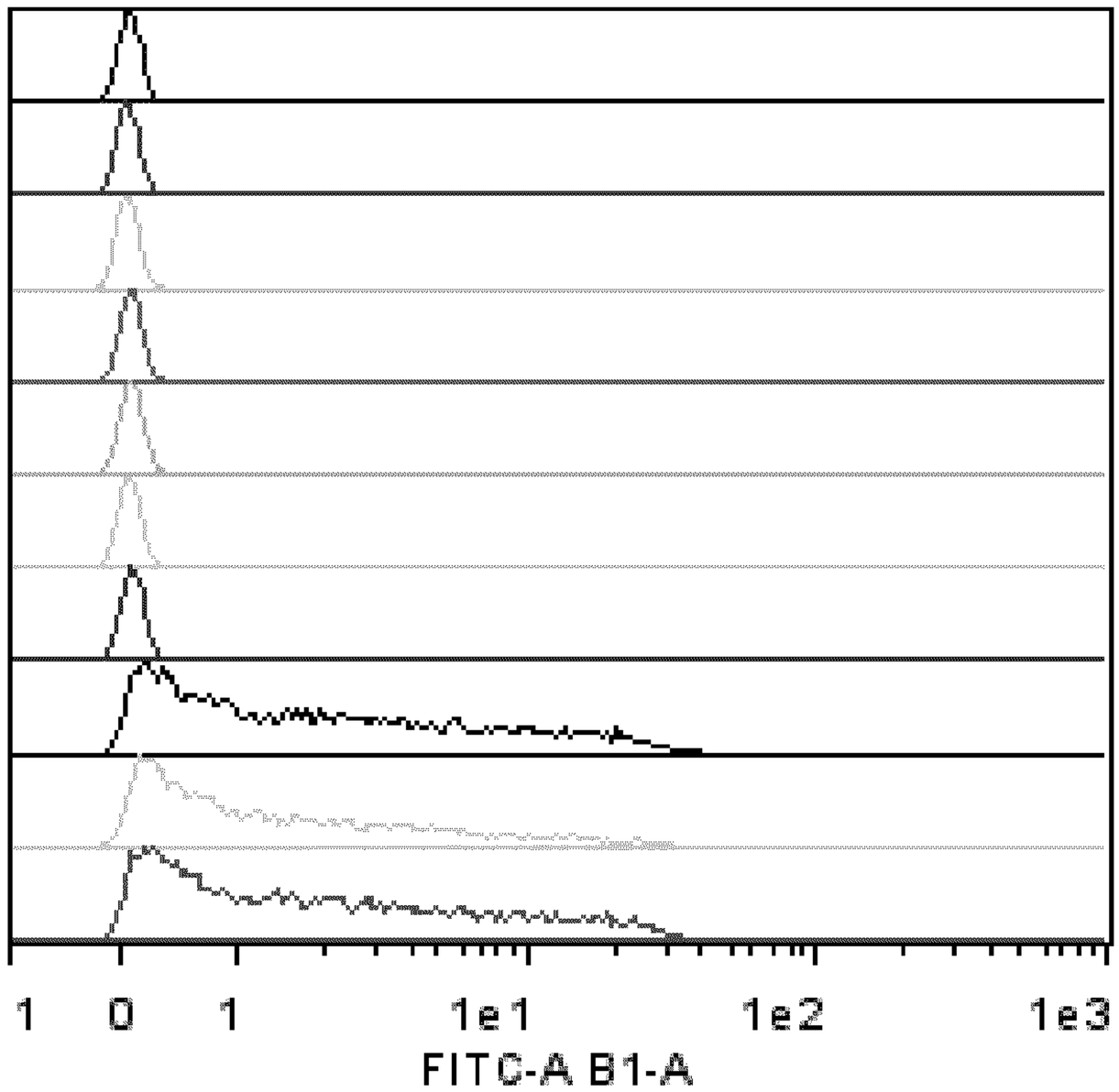
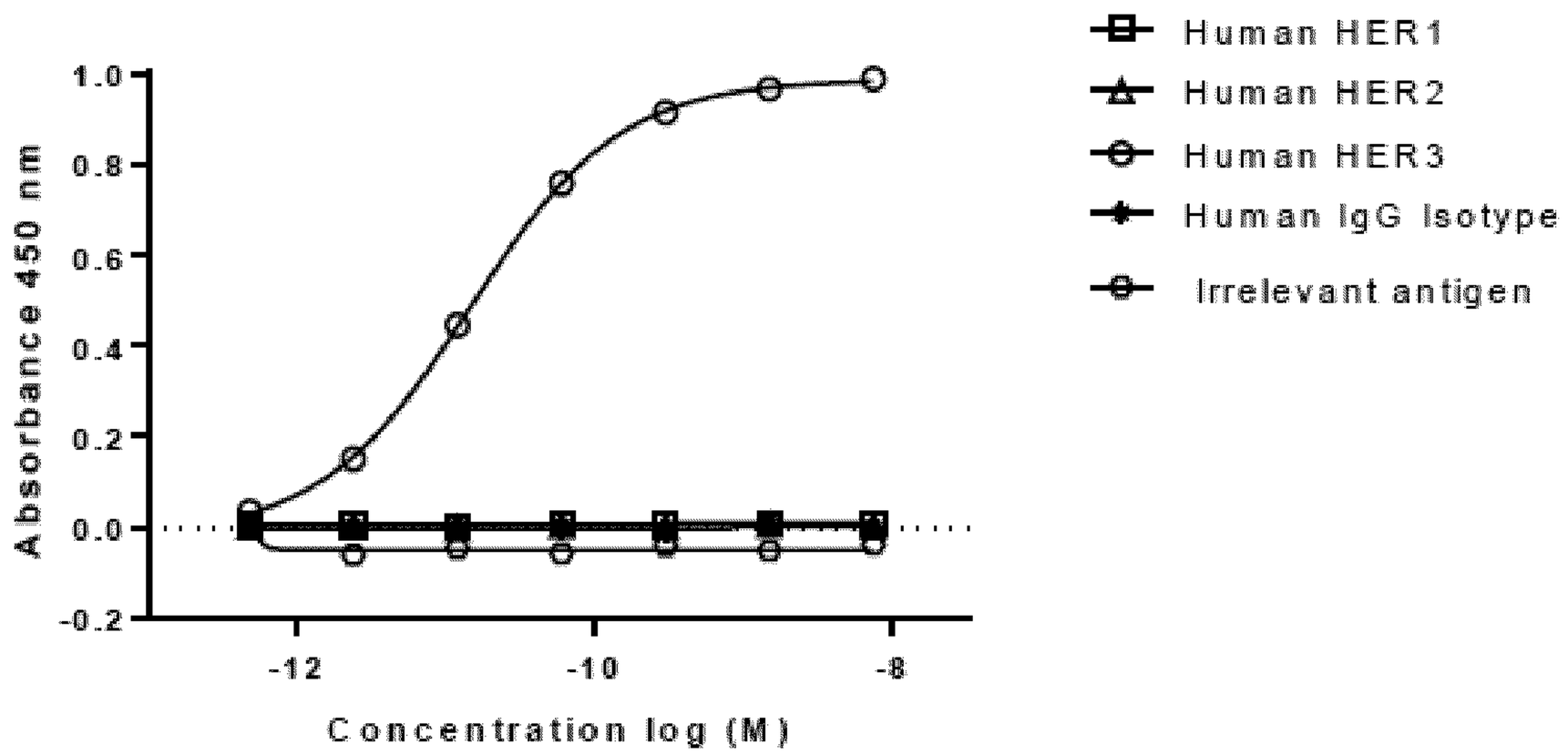

100%
75%
50%
25%
1
0
1
1e1
1e2
1e3
FITC-A B1-A
Color
Population
% Parent
HER3 positive [HEK293T WT: 10 ug 10D1F]
0.07
HER3 positive [HEK293T HER3 O/E: 10 ug 10D1F]
73.32

Figure 42A



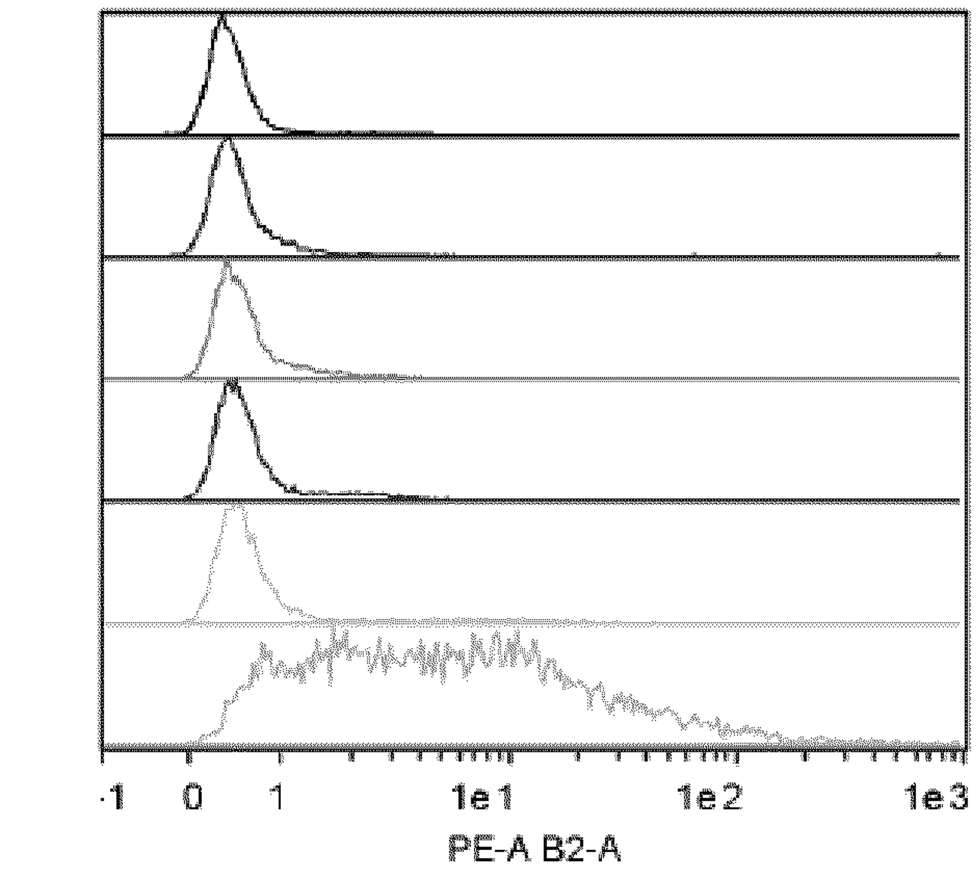
Color	Population	% Parent
	HER3 positive [HEK293T: unstained]	0.00
	HER3 positive [HEK293T WT: 10 ug hIgG1 Isotype]	0.07
	HER3 positive [HEK293T WT: 10 ug LJM716]	0.13
	HER3 positive [HEK293T WT: 10 ug 10D1P]	0.11
	HER3 positive [HEK293T WT: 10 ug 10D1F]	0.07
	HER3 positive [HEK293T HER3 O/E : unstained]	0.05
	HER3 positive [HEK293T HER3 O/E: 10 ug hIgG1 Isotype]	0.18
	HER3 positive [HEK293T HER3 O/E: 10 ug LJM716]	74.36
	HER3 positive [HEK293T HER3 O/E: 10 ug 10D1P]	65.74
	HER3 positive [HEK293T HER3 O/E: 10 ug 10D1F]	73.32

Figure 42B



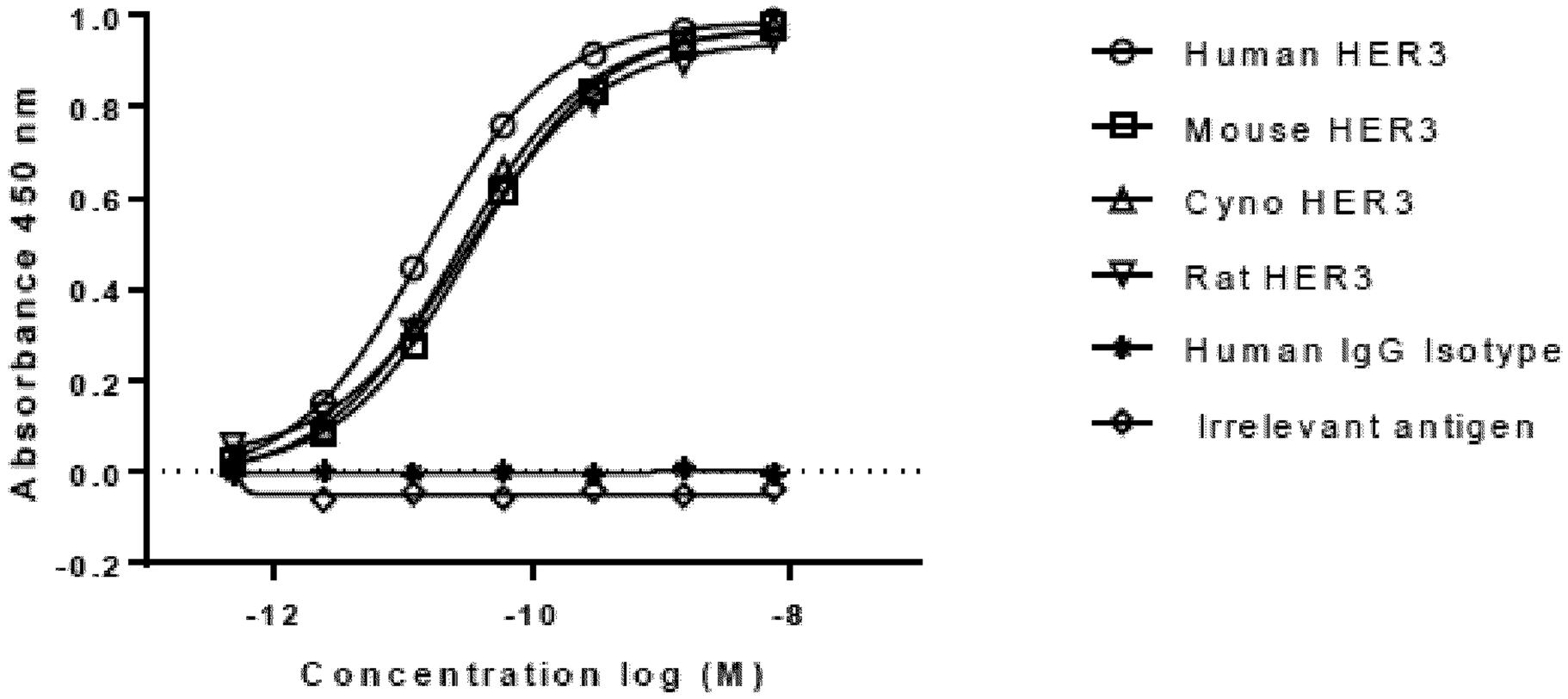
	Human EGFR	Human HER2	Human HER3
EC_{50} (M)	NA	NA	1.437e-011

Figure 43



	Antibody	% Positive for HER4
	Unstained	0
	Isotype	0.07
	10D1F.FcA	0.11
	LJM-716	0.27
	MM-121	8.73
	Commercial anti-HER4	50.86

Figure 44



	Human HER3	Mouse HER3	Rat HER3	Cyno HER3
EC_{50} (M)	1.437e-011	3.322e-011	3.032e-011	2.581e-011

Figure 45

Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
69	0.2882	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.3206	0.0063	2.05E-02	0.3202	99.9	0.0341	0.9902
35	0.1471	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.2068	0.0071	1.04E-02	0.2064	99.8	0.0341	0.9902
278	0.5458	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.513	0.0041	8.26E-02	0.5129	100	0.0341	0.9902
139	0.3968	7.26E-11	3.88E-10	2.97E+05	1.12E+04	2.16E-05	1.15E-04	0.3943	0.0046	4.13E-02	0.3941	99.9	0.0341	0.9902

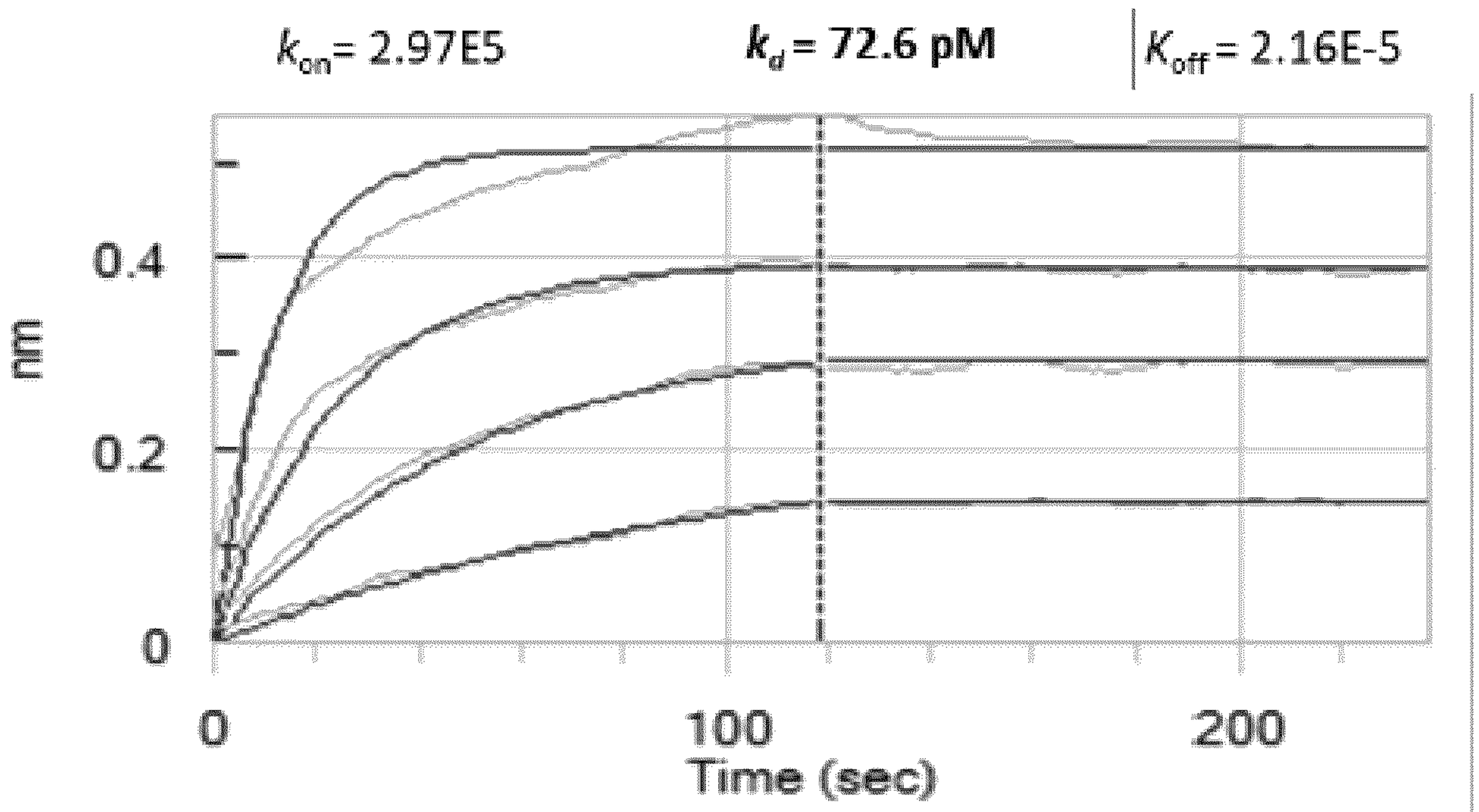


Figure 46A

Conc. (nM)	Response	KD (M)	KD Error	kon(1/Ms)	kon Error	kdis(1/s)	kdis Error	RMax	RMax Error	kobs(1/s)	Req	Req/Rmax(%)	Full X^2	Full R^2
242	0.4624	2.22E-11	2.70E-11	2.23E+05	3.28E+03	4.96E-06	6.03E-06	0.4468	0.001	5.40E-02	0.4467	100	0.0108	0.999
121	0.2437	2.22E-11	2.70E-11	2.23E+05	3.28E+03	4.96E-06	6.03E-06	0.2478	0.001	2.70E-02	0.2478	100	0.0108	0.999
60.5	0.0679	2.22E-11	2.70E-11	2.23E+05	3.28E+03	4.96E-06	6.03E-06	0.0869	0.0009	1.35E-02	0.0868	100	0.0108	0.999
30.3	0.0208	2.22E-11	2.70E-11	2.23E+05	3.28E+03	4.96E-06	6.03E-06	0.0469	0.0011	6.77E-03	0.0468	99.9	0.0108	0.999

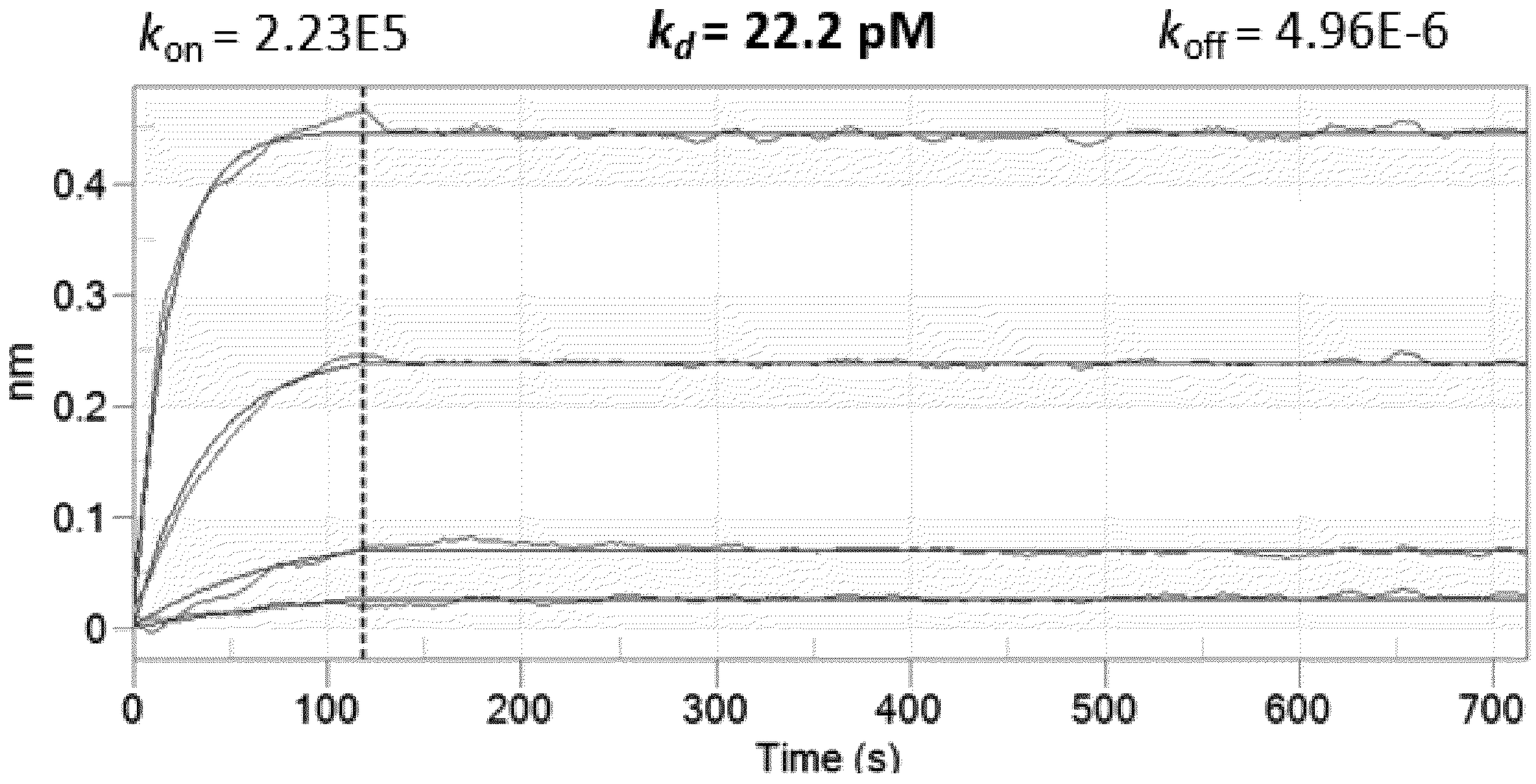
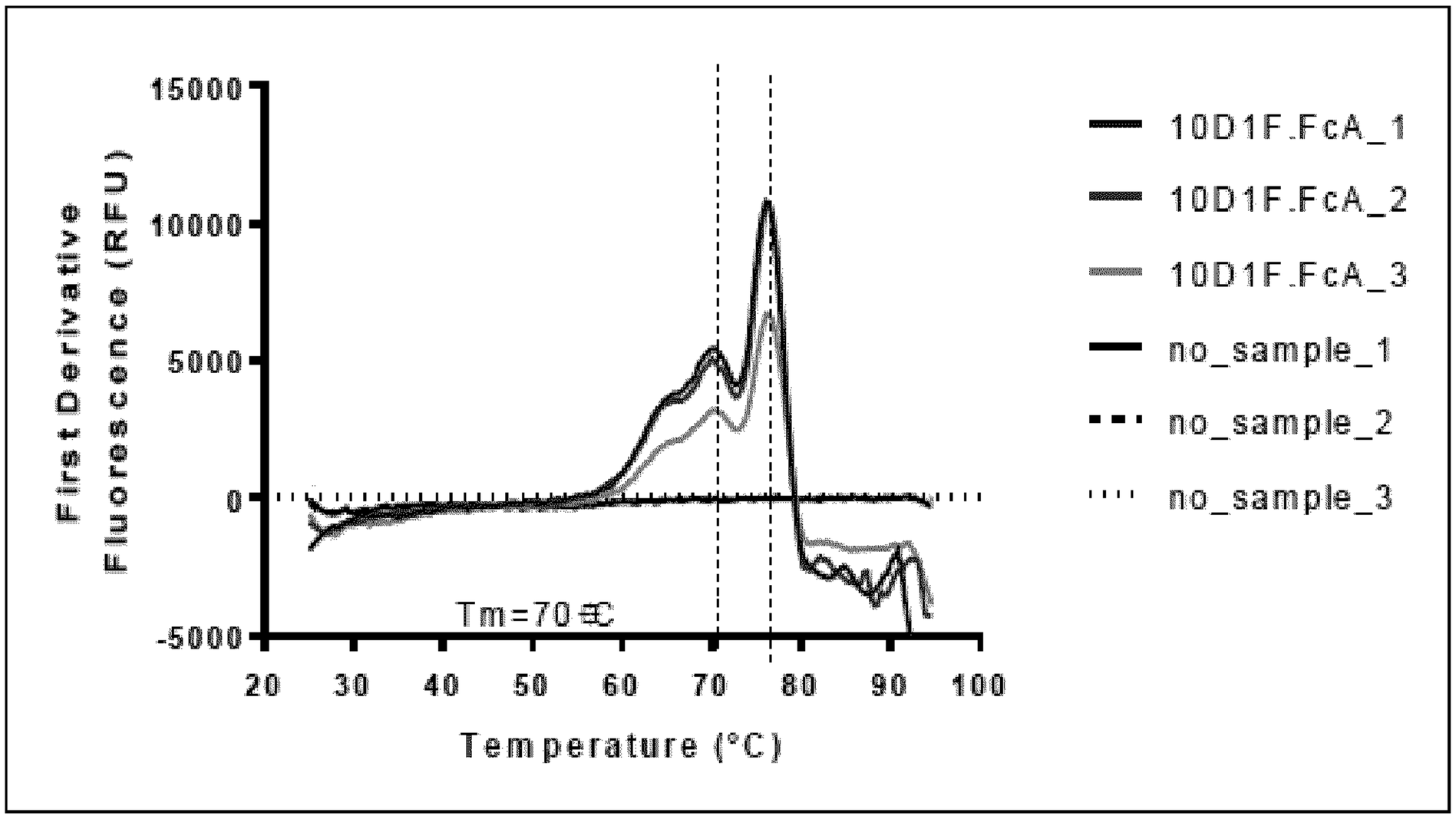
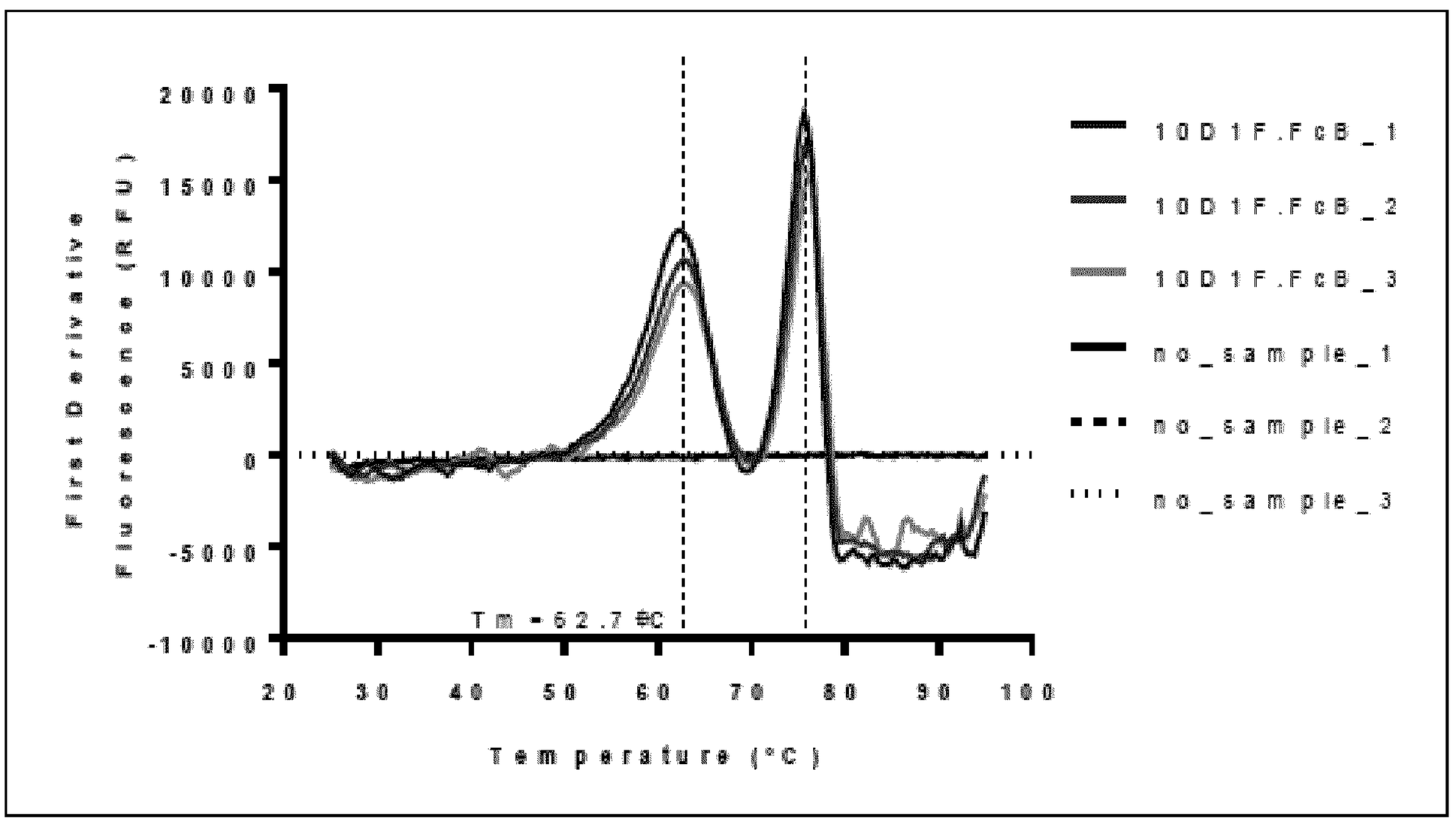


Figure 46B



	Tm1 (°C)	Tm2 (°C)
HMBD-001-10D1F.FcA	70.0	76.8

Figure 47A



	Tm1 (°C)	Tm2 (°C)
HMBD-001-10D1F.FcB	62.7	76.0

Figure 47B

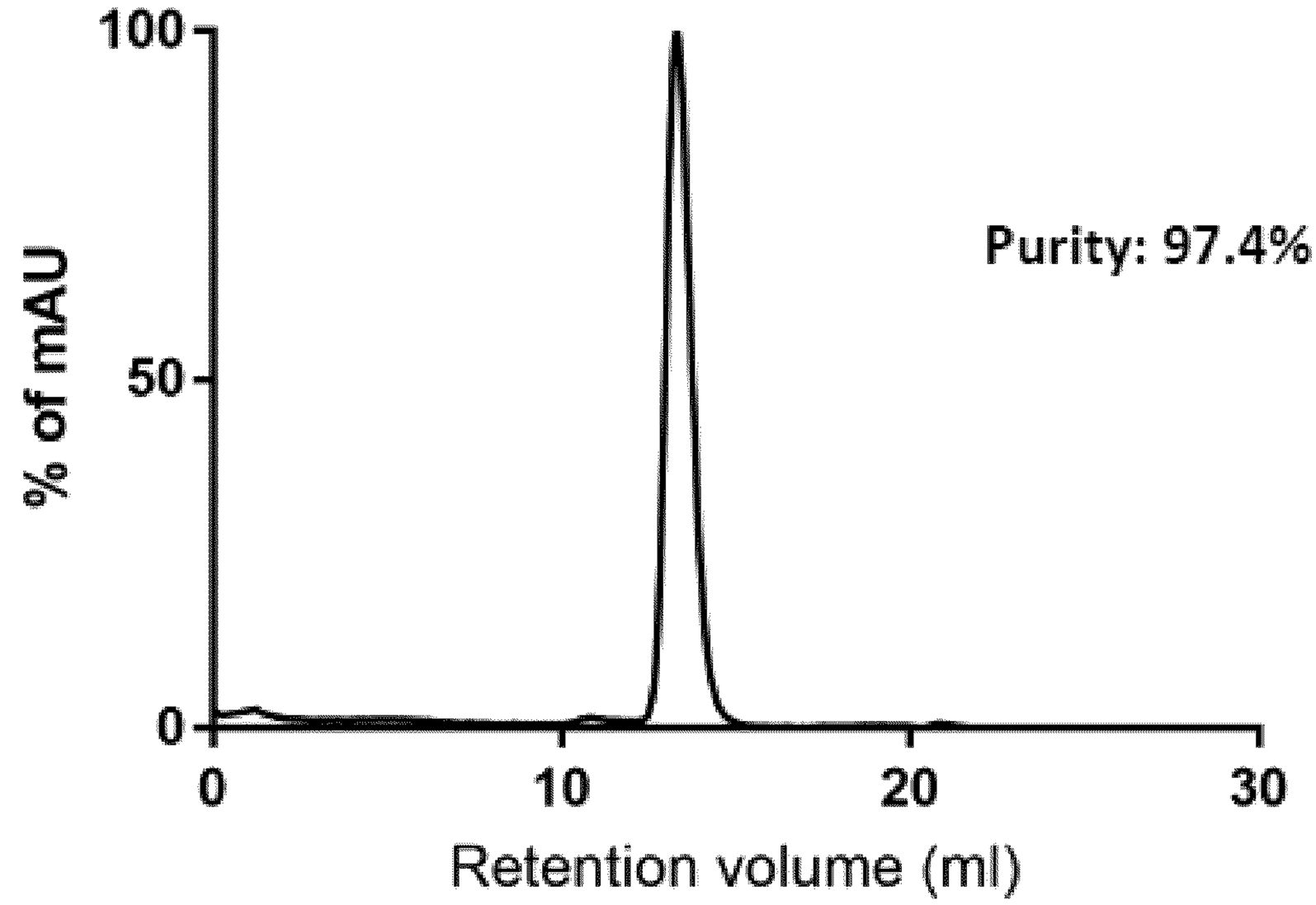


Figure 48A

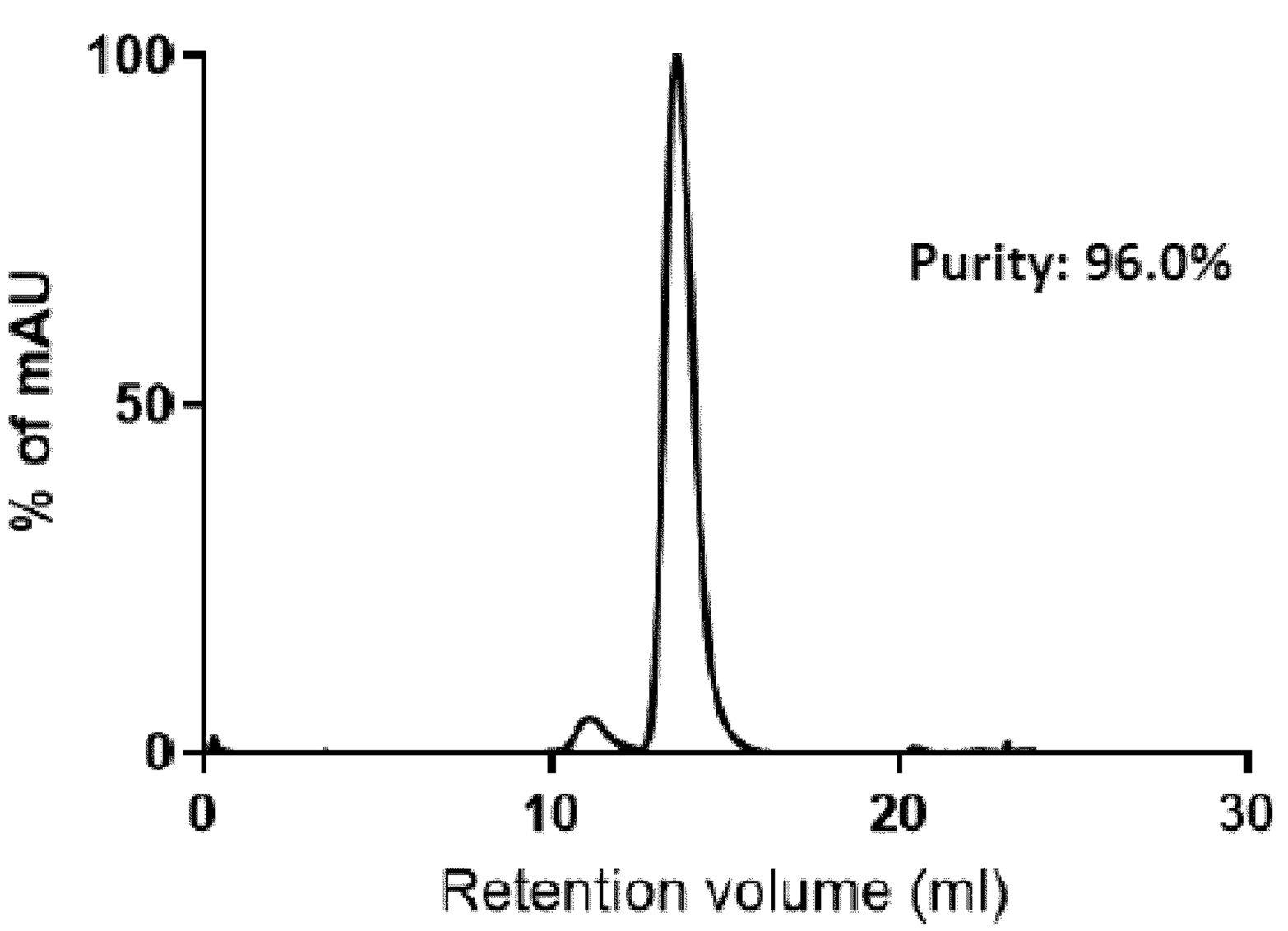


Figure 48B

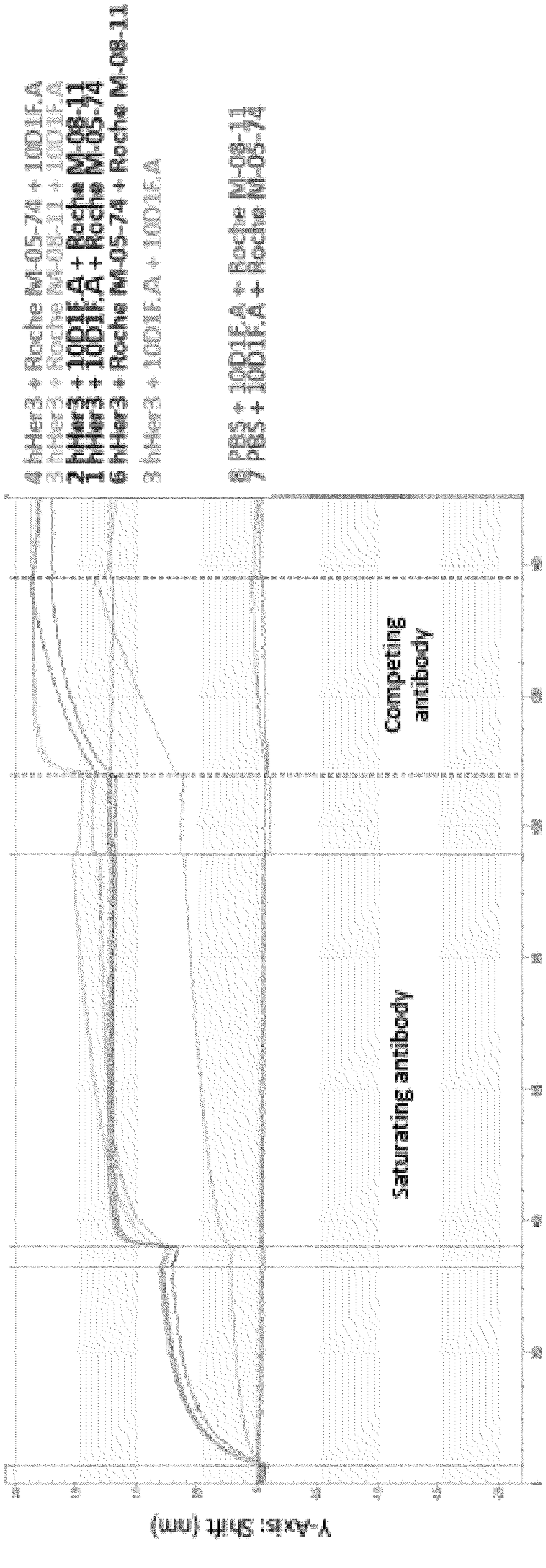

4 hHer3 + Roche M-05-74 + 10D1F.A
2 hHer3 + 10D1F.A + Roche M-08-11
1 hHer3 + 10D1F.A + Roche M-05-74
6 hHer3 + Roche M-05-74 + Roche M-08-11
3 hHer3 + 10D1F.A + 10D1F.A
8 PBS + 10D1F.A + Roche M-08-11
7 PBS + 10D1F.A + Roche M-05-74
Competing antibody
Saturating antibody
X-Axis: Time (s)
Y-Axis: Shift (nm)

Figure 49A

		Competing Antibody		
Saturating Antibody		10D1	Roche M-05-74	Roche M-08-11
	10D1	X	0.5084	0.5614
	Roche M-05-74	0.5023	X	0.6424
	Roche M-08-11	0.4114	x	x

Figure 49B

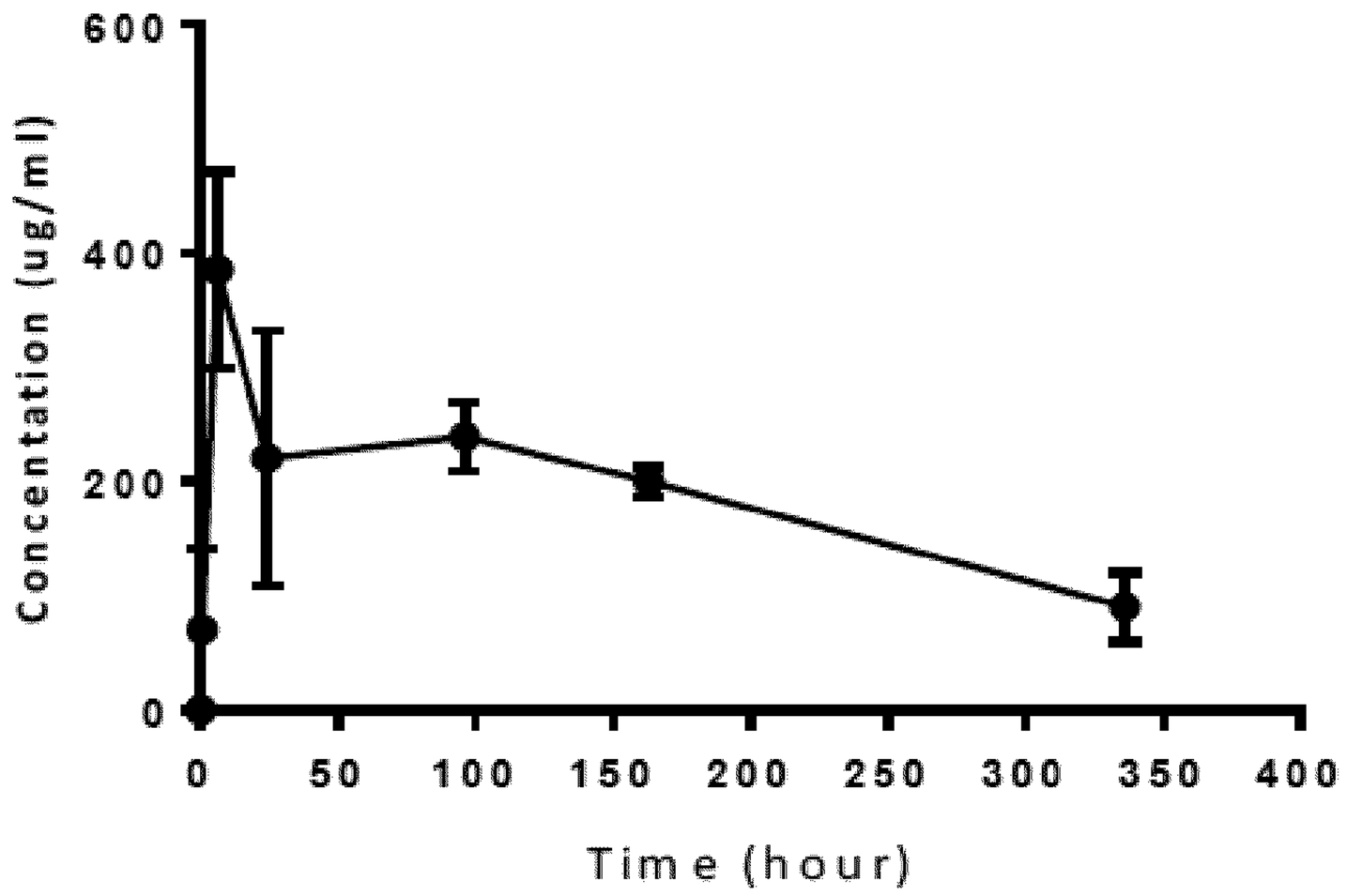


Figure 50

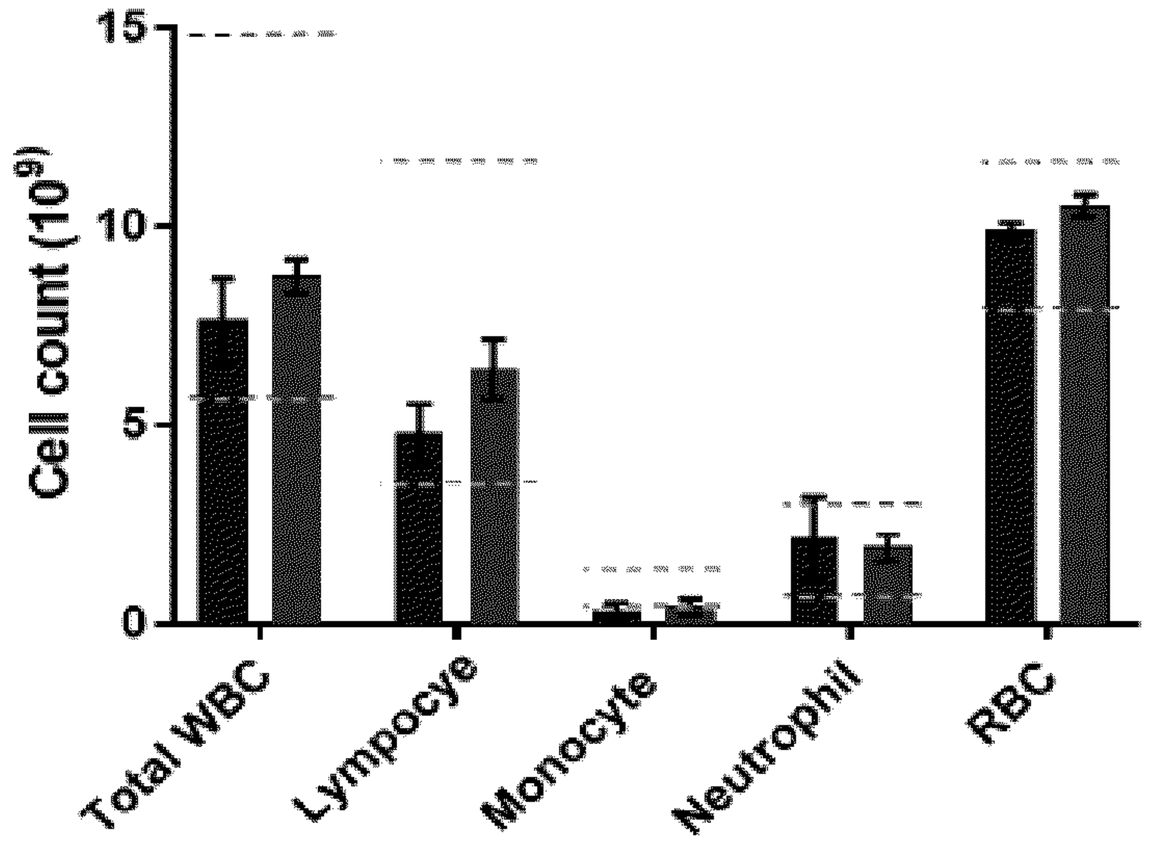


Figure 51A

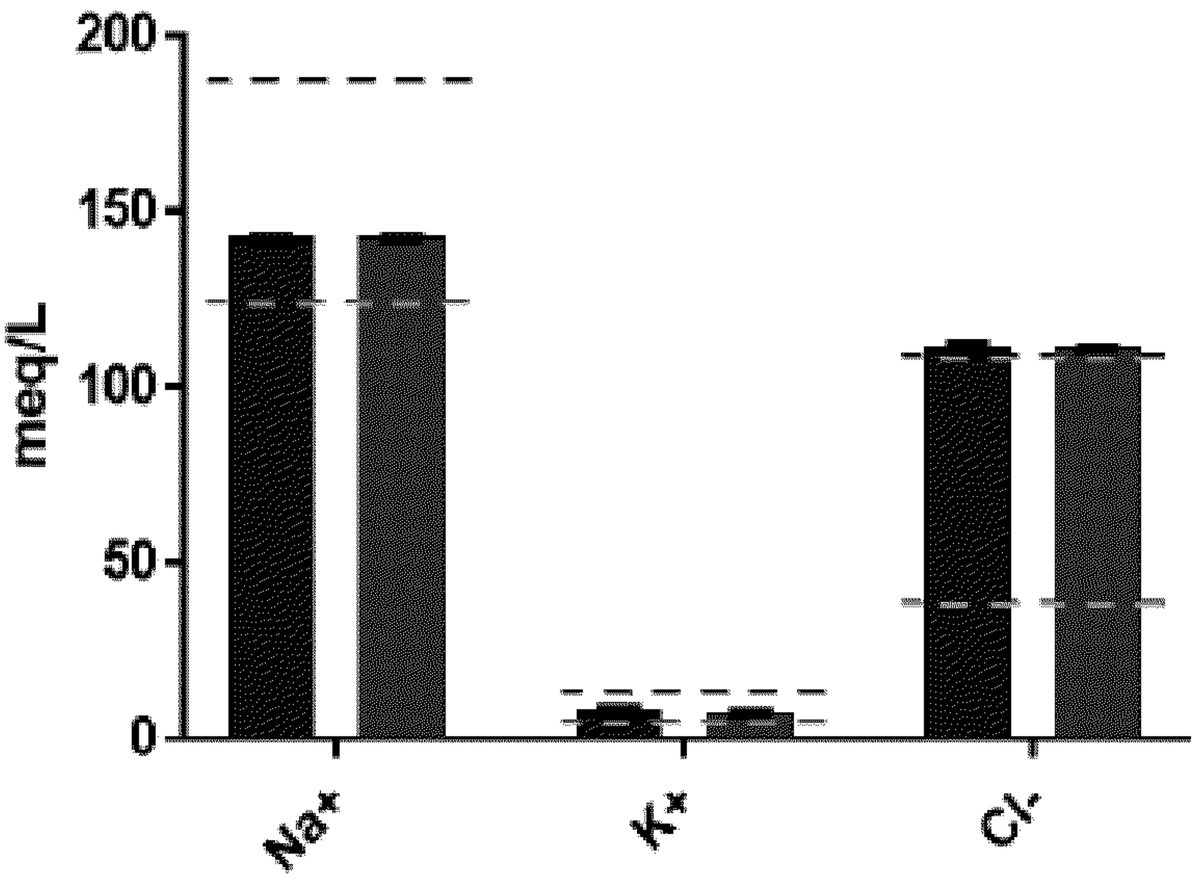


Figure 51B

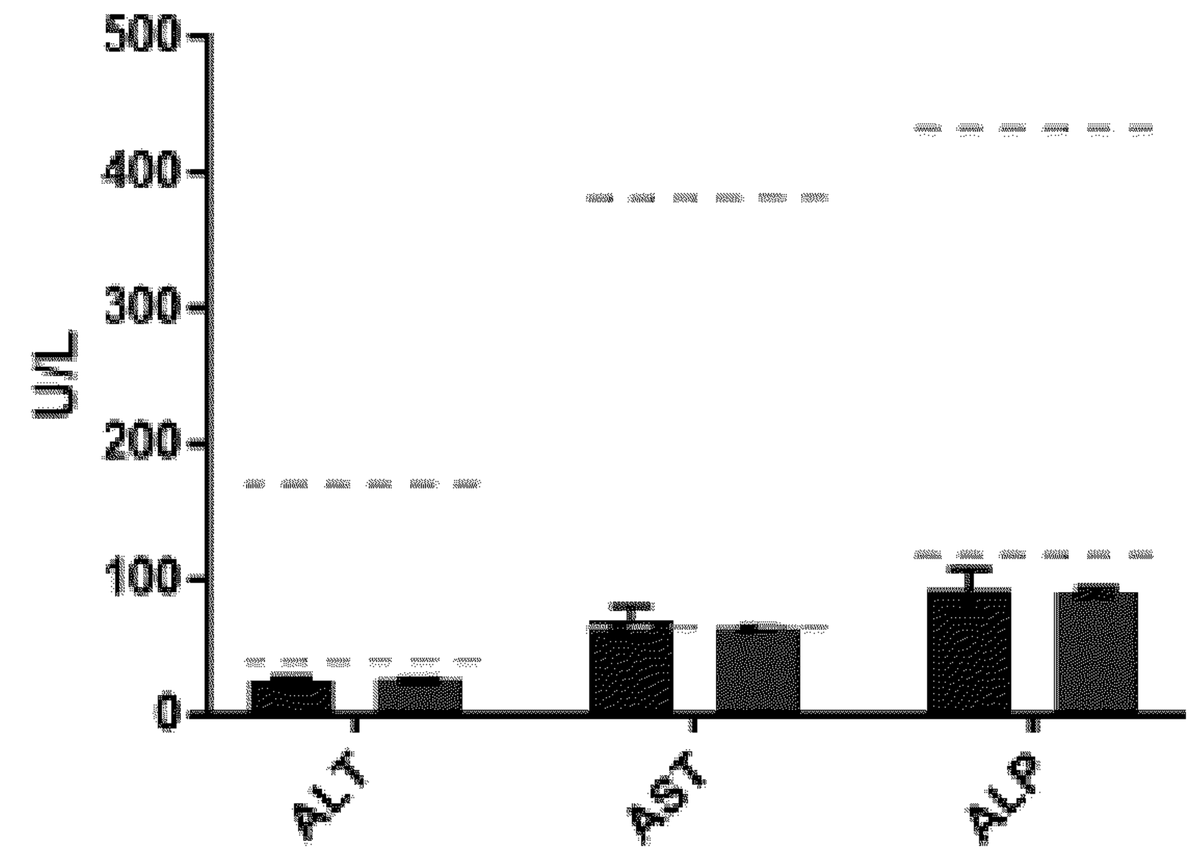


Figure 51C

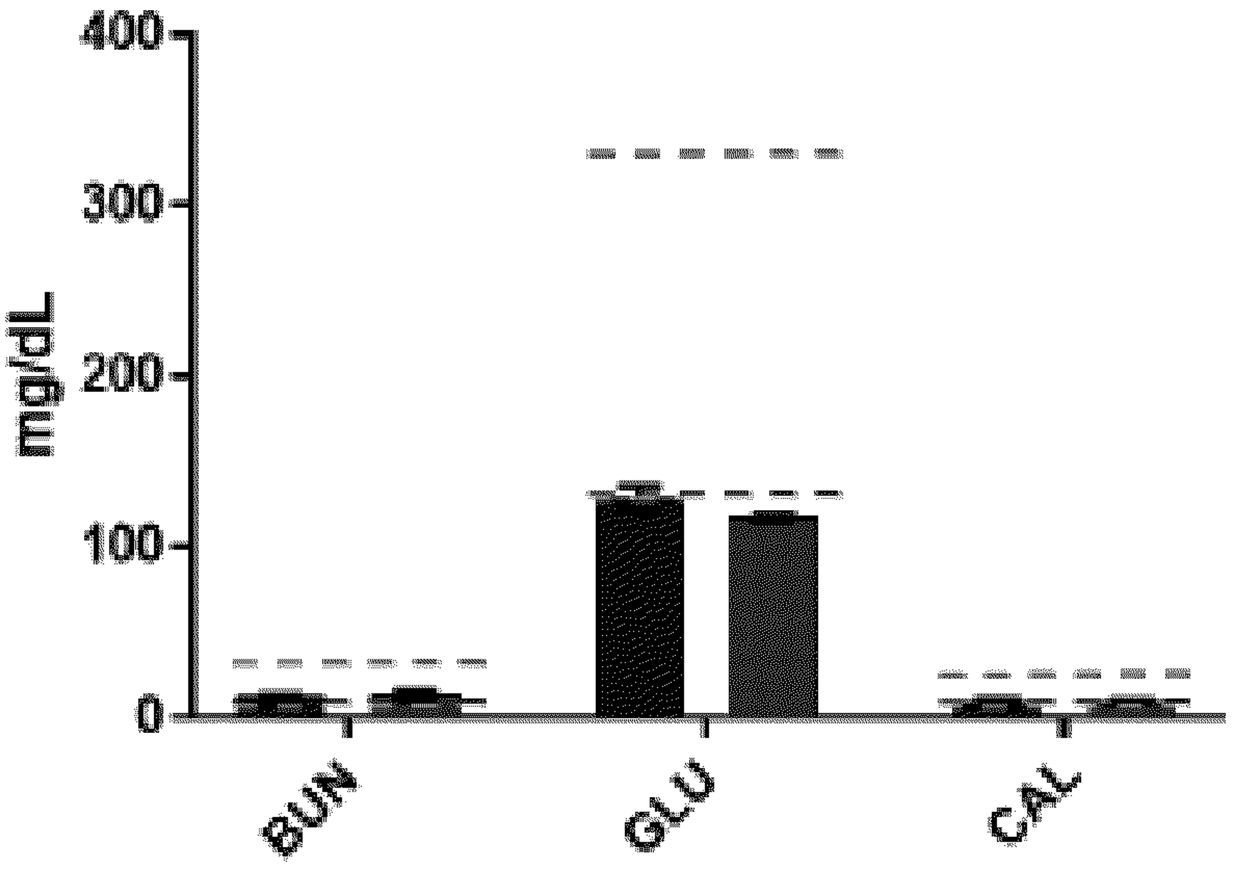


Figure 51D

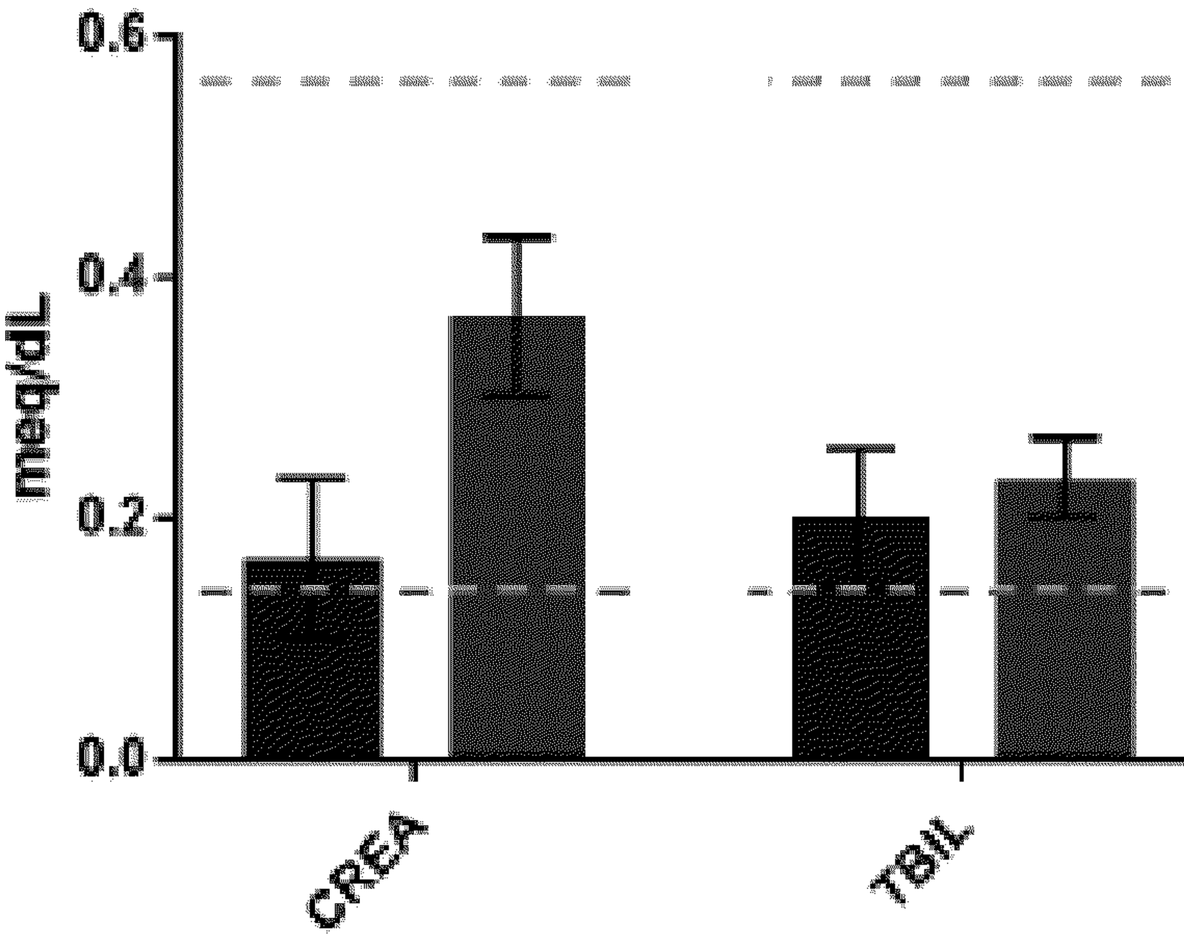


Figure 51E

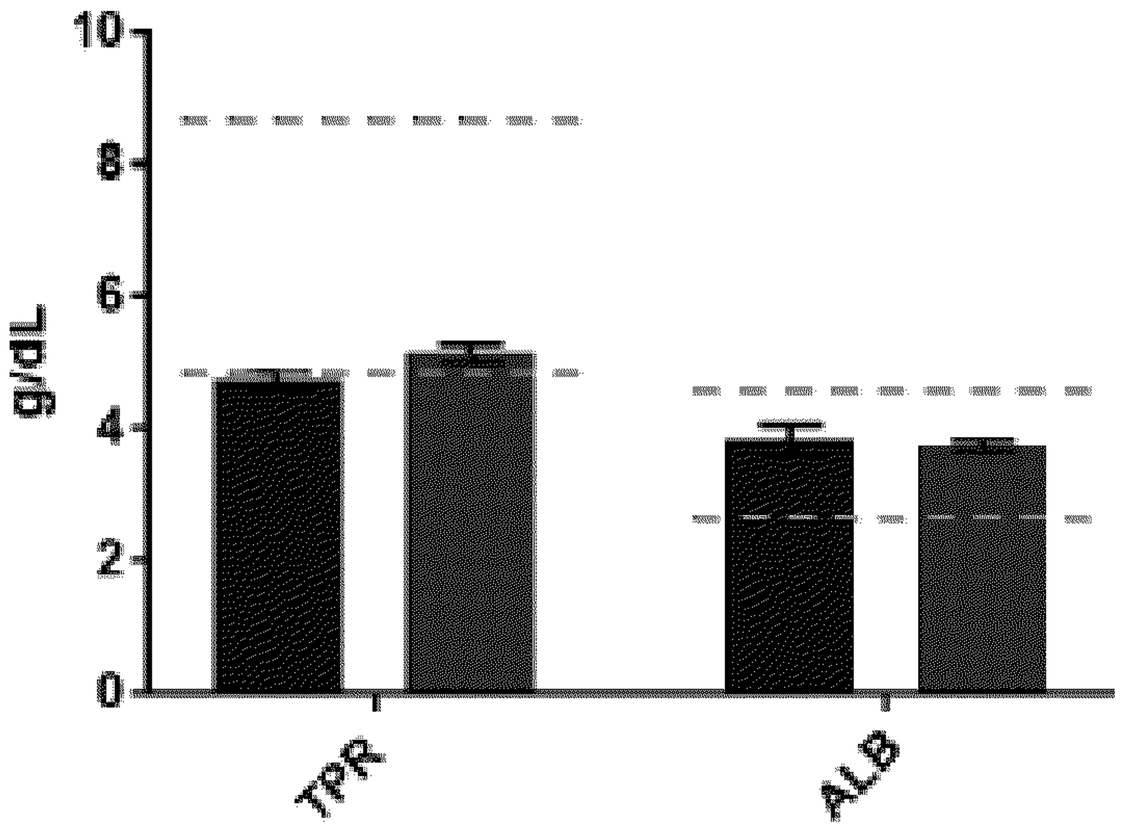
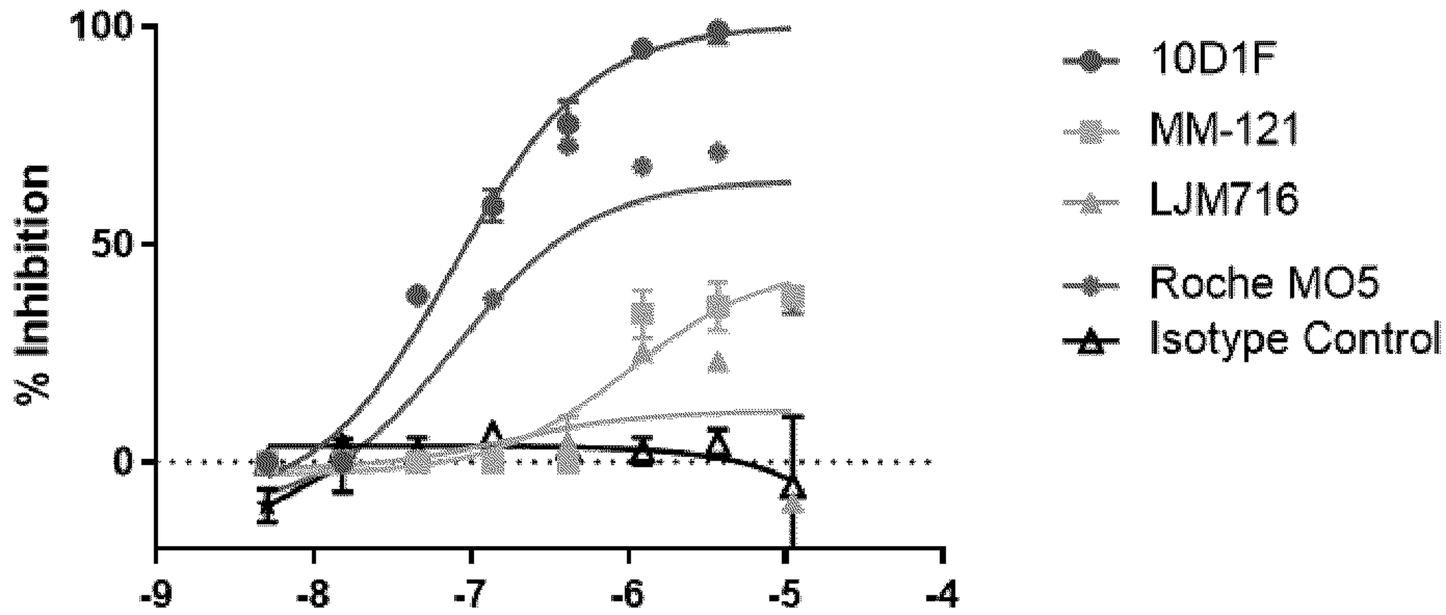
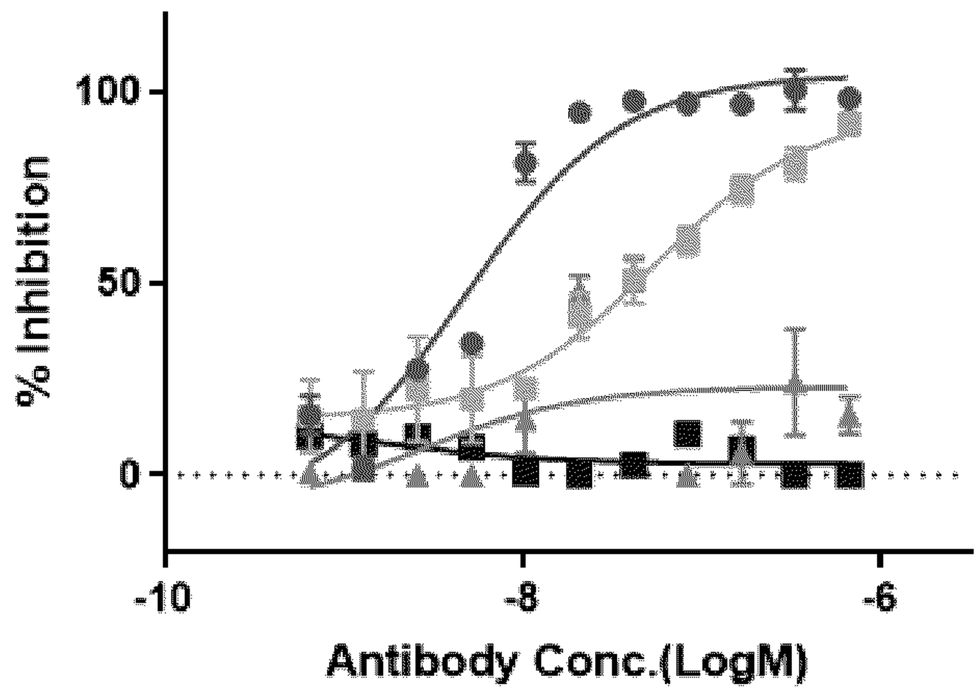


Figure 51F



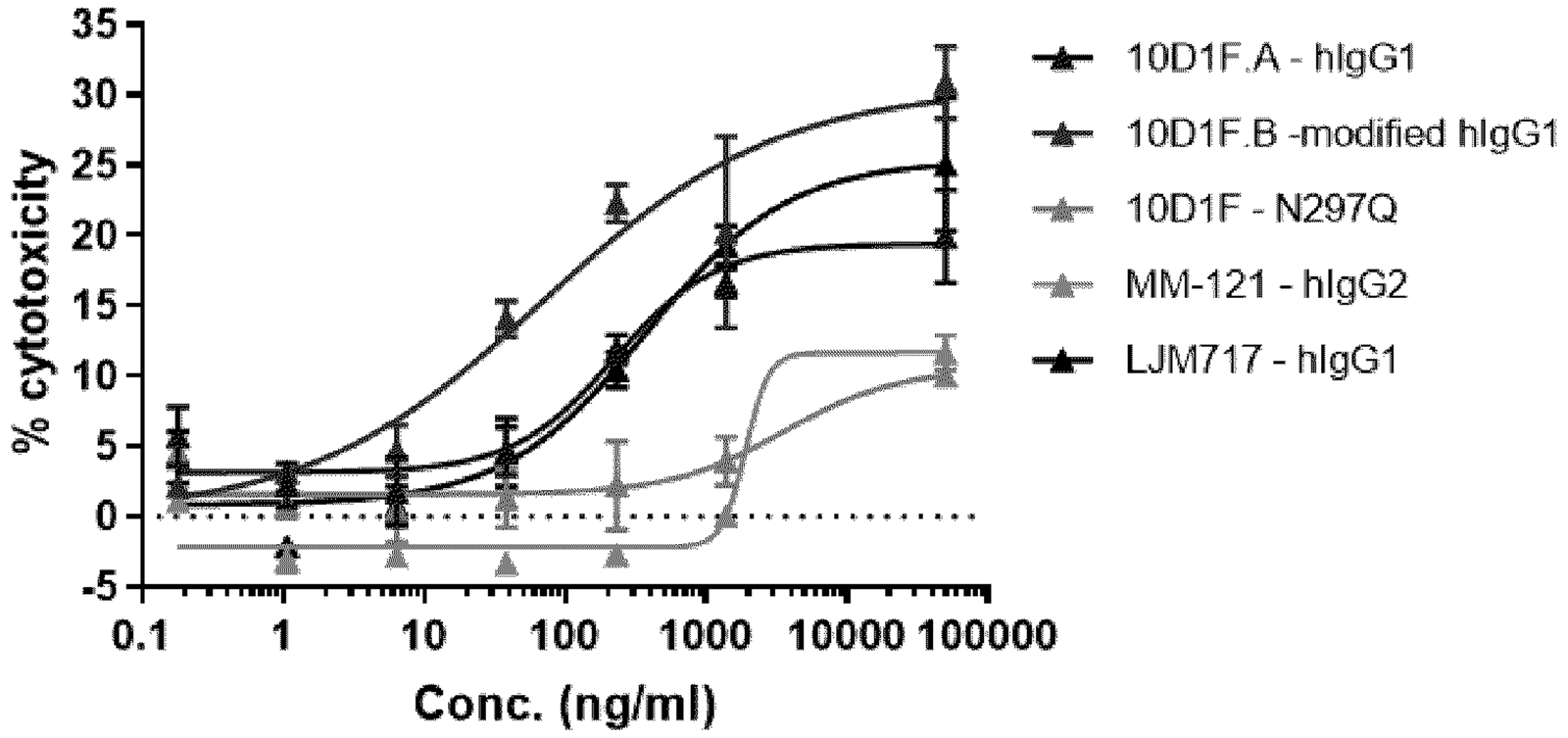
	10D1F	MM-121	LJM-716	Roche M05	Isotype Control
HER2:HER3 IC_{50} (M)	7.88e-008	N.A.	N.A.	8.025e-008	N.A.

Figure 52



	10D1F	MM-121	LJM-716	Isotype Control
EGFR:HER3 IC_{50} (M)	4.781e-009	5.419e-008	N.A.	N.A.

Figure 53



	10D1F.FcA 10D1F hIgG1	10D1F.FcB 10D1F hIgG1 GASDALIE-LCKC	10D1F hIgG1 N297Q	SBT hIgG2	LJM716 hIgG1
EC_{50} (ng/ml)	224.4	68.96	NA	NA	377.3

Figure 54

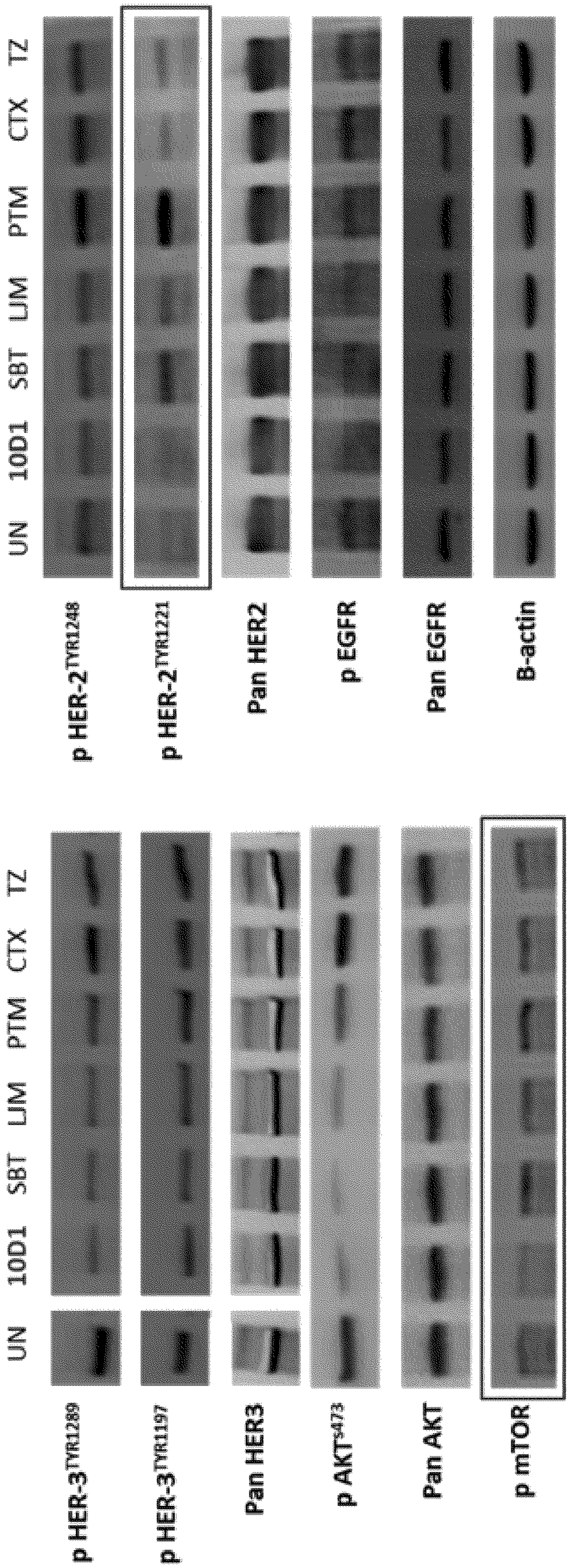
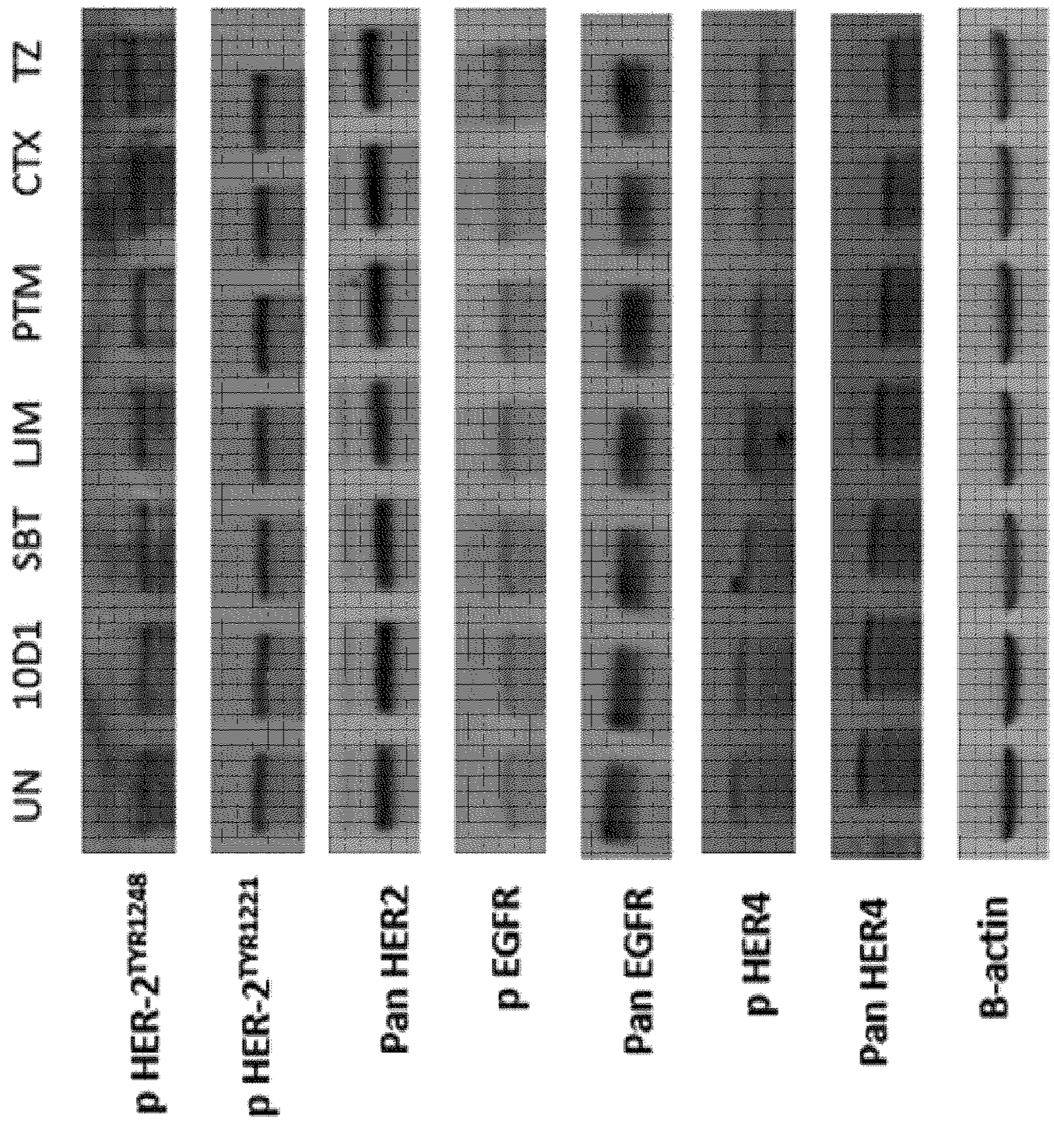
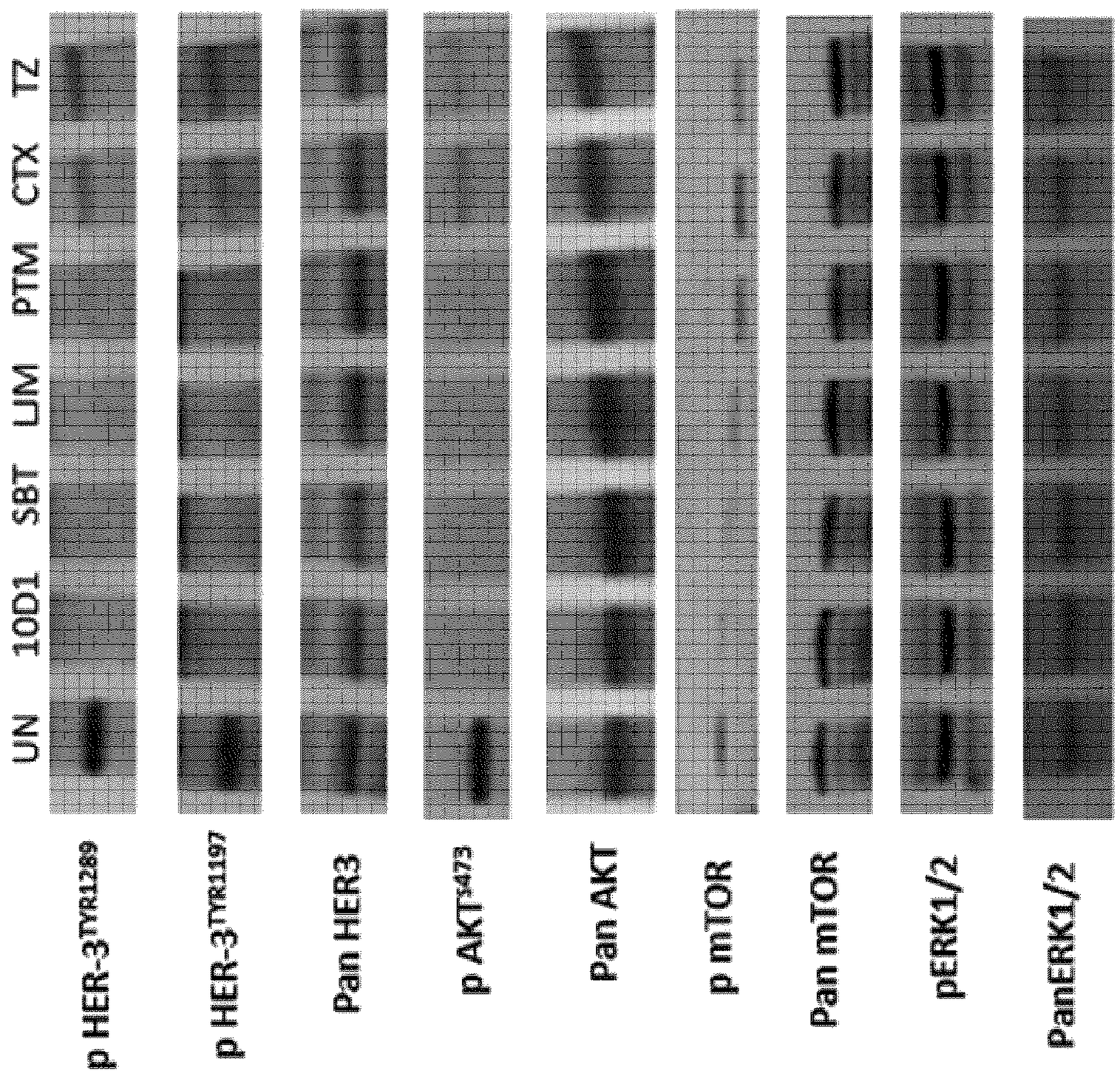

UN
10D1
SBT
LIM
PTM
CTX
TZ
p HER-2TYR1248
p HER-2TYR1221
Pan HER2
p EGFR
Pan EGFR
B-actin
Legend:
UN = Untreated
10D1 = 10D1F.A
SBT = Seribantumab (MM-121)
LIM = Elgemtumab (LIM-716)
PTM = Pertuzumab
CTX = Cetuximab
TZ = Trastuzumab
p HER-3TYR1289
p HER-3TYR1197
Pan HER3
p AKTS473
Pan AKT
p mTOR
Pan mTOR
pERK1/2
PanERK1/2

Figure 55A


UN
10D1
SBT
LIM
PTM
CTX
TZ
p HER-2TYR1248
p HER-2TYR1221
Pan HER2
p EGFR
Pan EGFR
p HER4
Pan HER4
B-actin
Legend:
UN = Untreated
10D1 = 10D1F.FcA
SBT = MM-121
LIM = LM-716
PTM = Pertuzumab
CTX = Cetuximab
TZ = Trastuzumab

55B

Figure


UN
10D1
SBT
LIM
PTM
CTX
TZ
p HER-3TYR1289
p HER-3TYR1197
Pan HER3
p AKTS473
Pan AKT
p mTOR
Pan mTOR
pERK1/2
PanERK1/2

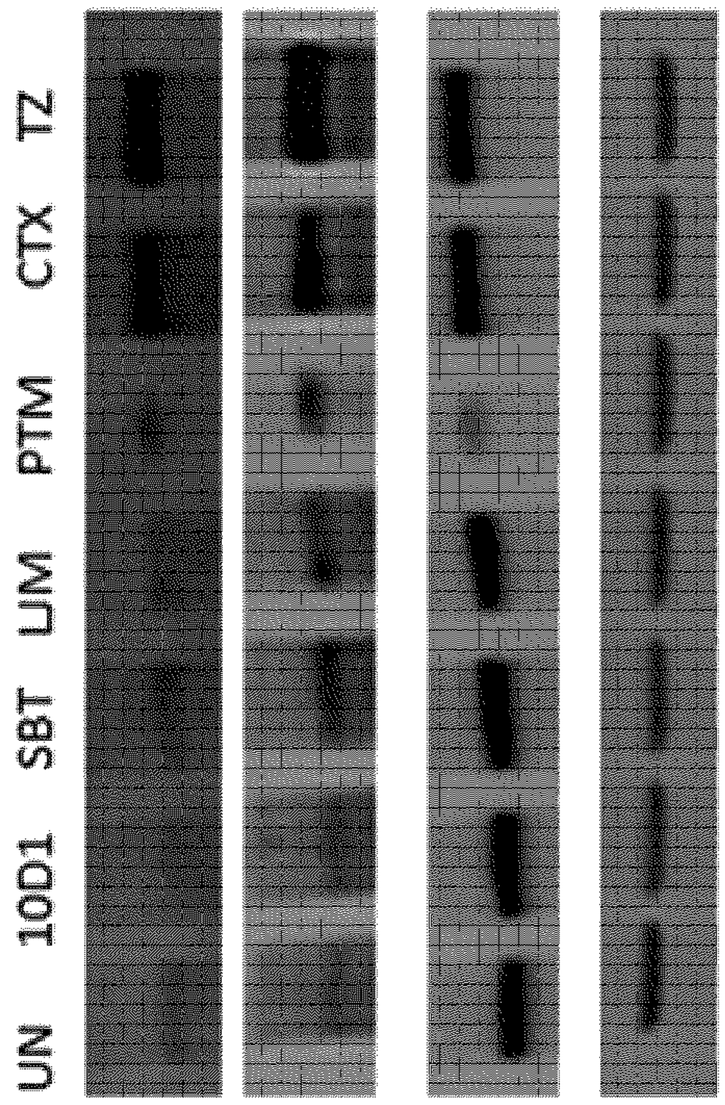
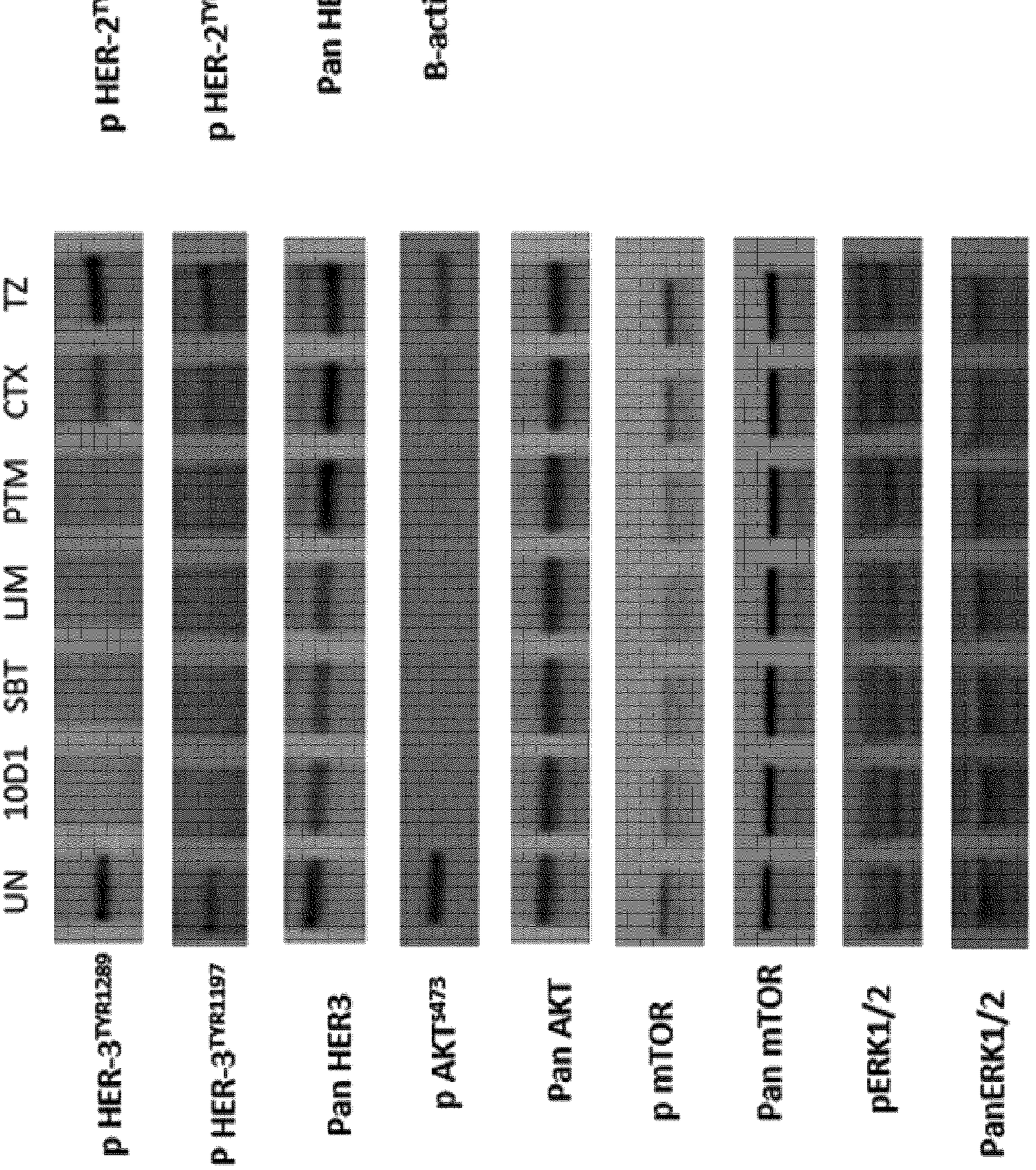
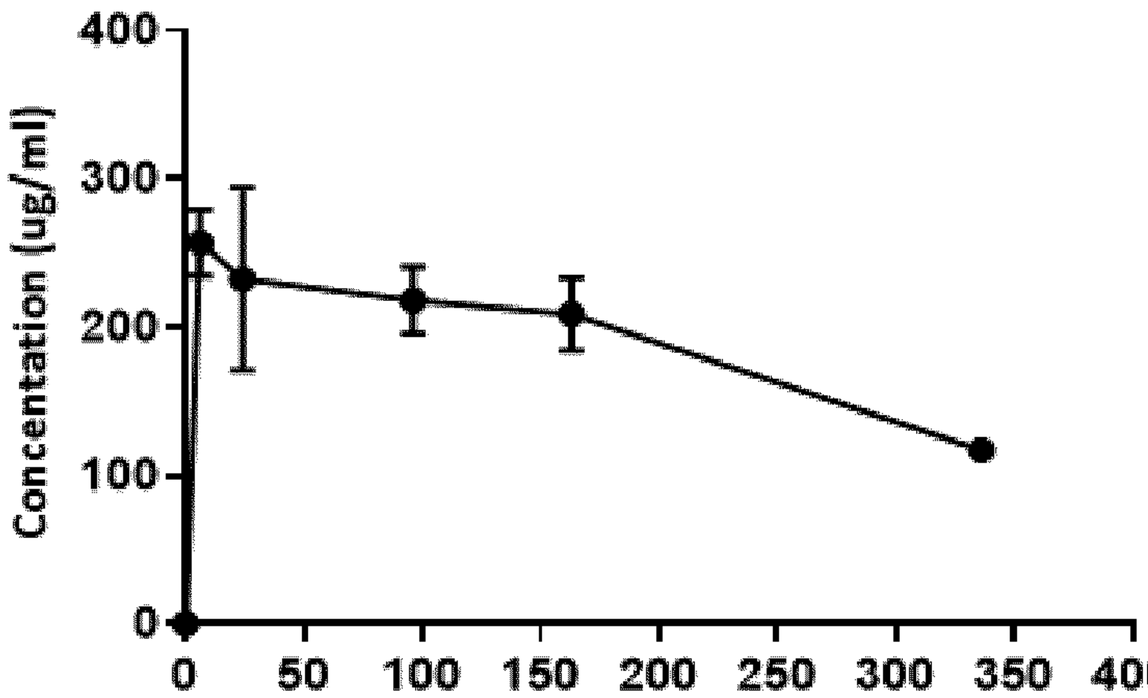

UN
10D1
SBT
LIM
PTM
CTX
TZ
p HER-2TYR1248
p HER-2TYR1221
Pan HER2
B-actin
Legend:
UN = Untreated
10D1 = 10D1F.FcA
SBT = MM-121
LIM = LIM-716
PTM = Pertuzumab
CTX = Cetuximab
TZ = Trastuzumab

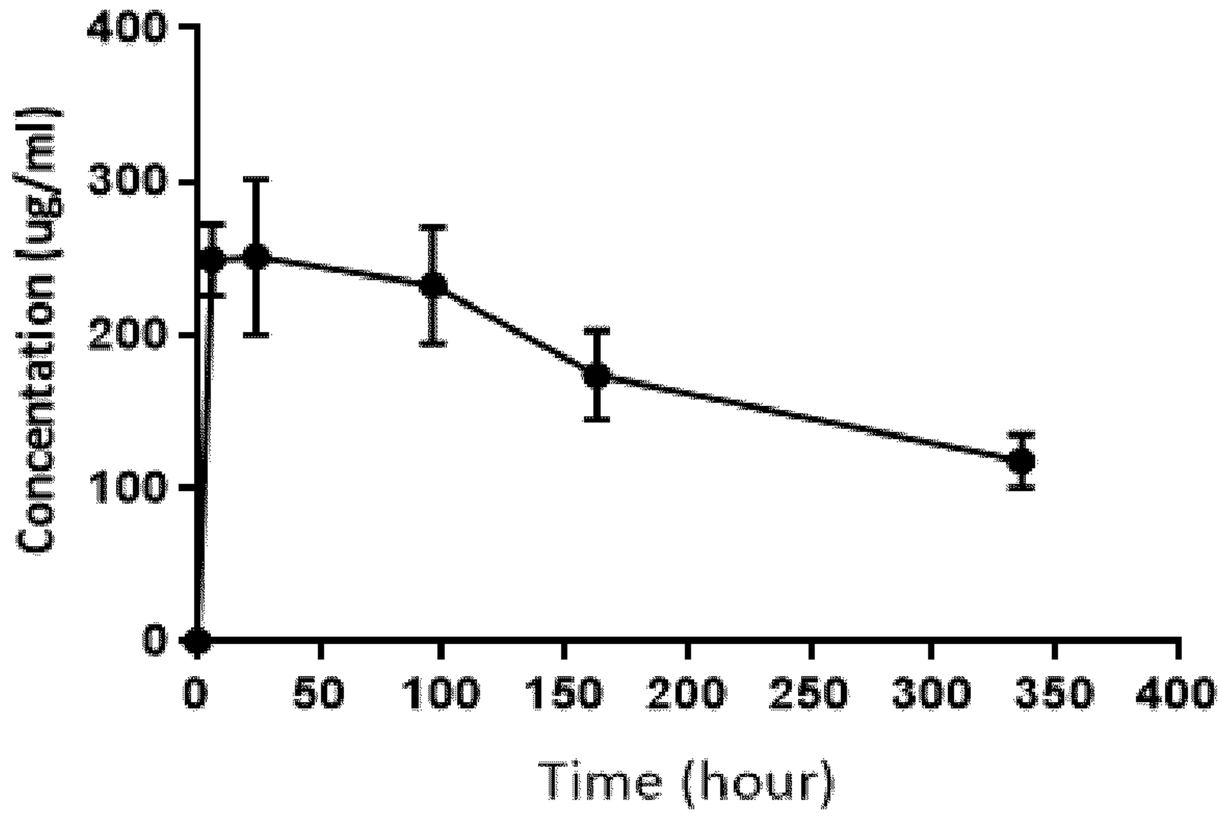
Figure 55C


UN
10D1
SBT
LIM
PTM
CTX
TZ
p HER-3TYR1289
P HER-3TYR1197
Pan HER3
p AKT473
Pan AKT
p mTOR
Pan mTOR
pERK1/2
PanERK1/2



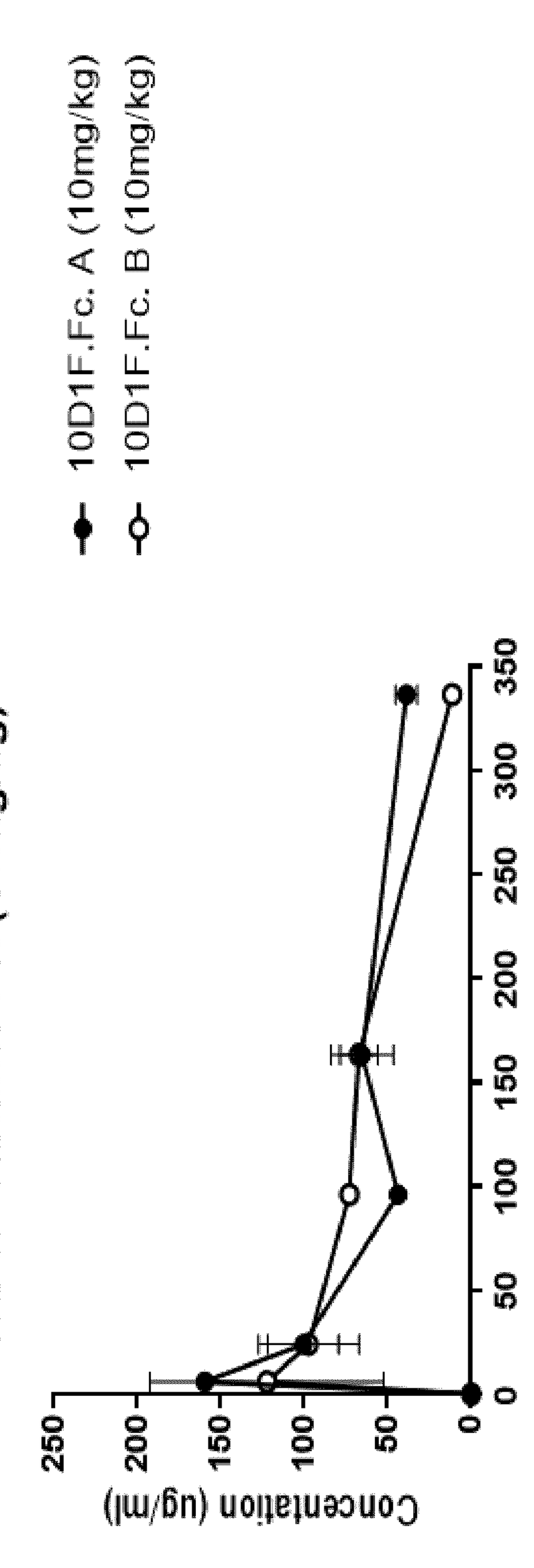
Cmax (ug/ml)	Tmax (hr)	AUC0-336 (ug*h/ml)	AUC0-Infinity (ug*h/ml)	Elimination Rate KEL(h-1)	T1/2 (hr)	CL (ml/h)	Vd (mL/kg)
257.297	6.000	64677.050	107359.970	0.003	252.753	0.005	1.697

Figure 56A



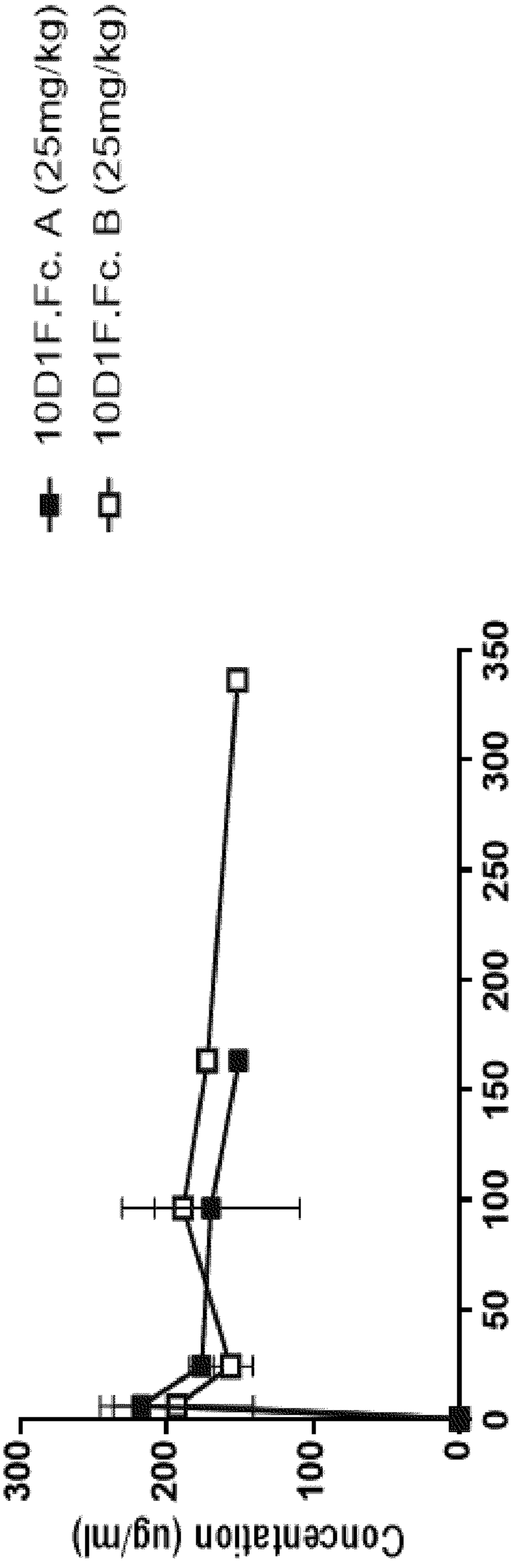
Cmax (ug/ml)	Tmax (hr)	AUC0-336 (ug*h/ml)	AUC0-Infinity (ug*h/ml)	Elimination Rate KEL(h-1)	T1/2 (hr)	CL (ml/h)	Vd (mL/kg)
250.673	24.000	62163.226	108529.704	0.003	273.167	0.005	1.804

Figure 56B



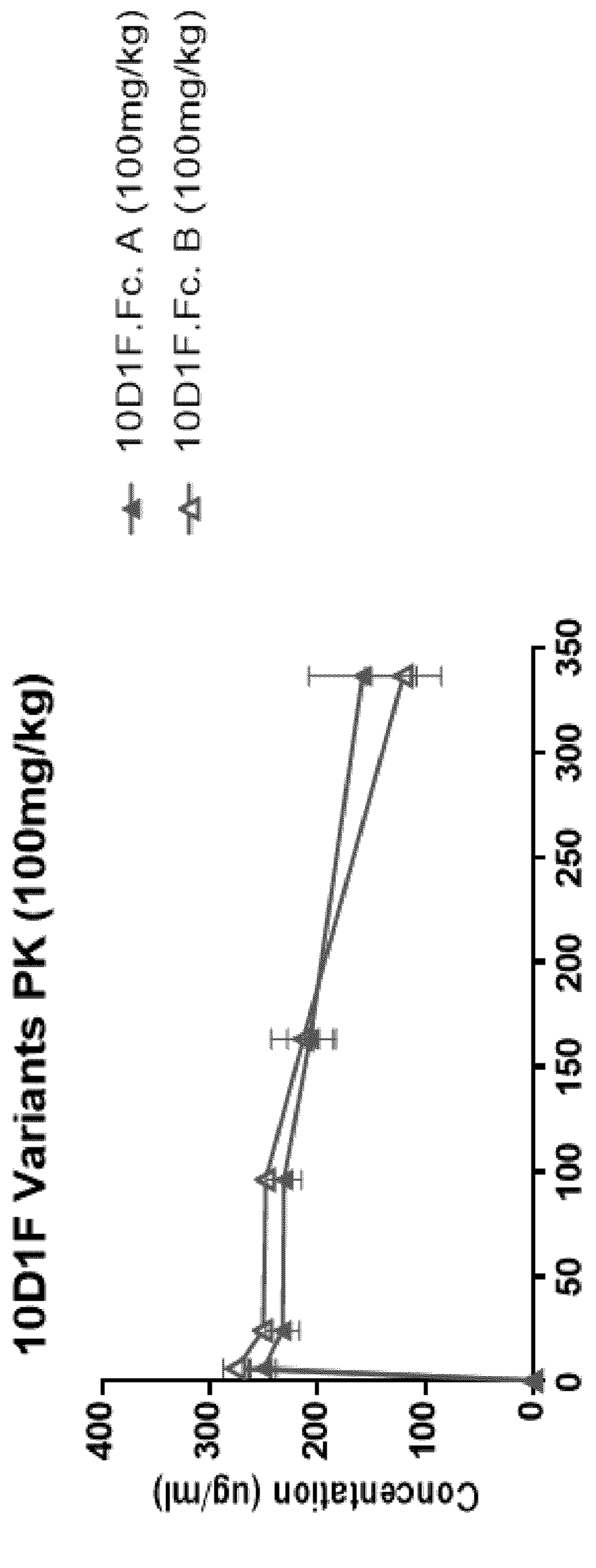
Arms	Dose	Cmax (ug/ml)	Tmax (hr)	AUC0-336 (ug*h/ml)	AUC0-Infinity (ug*h/ml)	T1/2 (hr)	CL (ml/h)	Vd (mL/kg)
10D1F.Fc.A	10 mg/kg	159.851	6.000	21286.213	32543.407	199.434	0.077	23.273
10D1F.Fc.B	10 mg/kg	122.573	6.000	20585.915	22289.688	102.642	0.112	15.741

Figure 57A



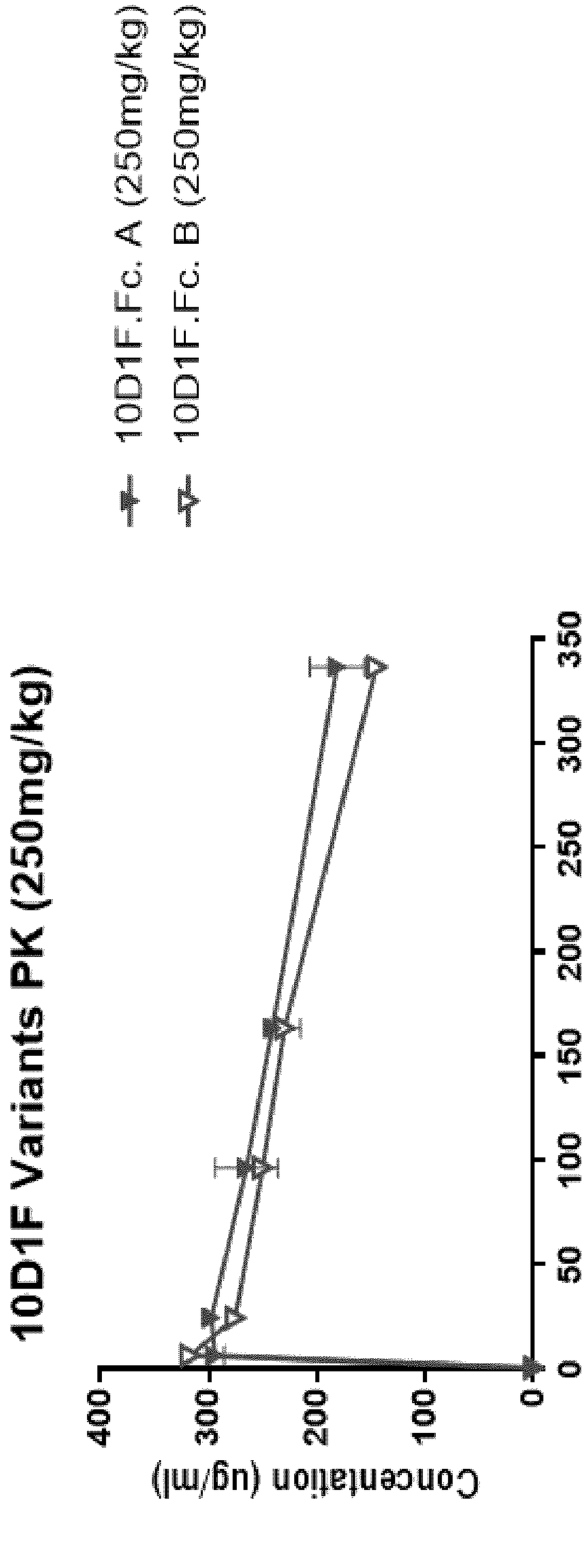
Arms	Dose	Cmax (ug/ml)	Tmax (hr)	AUC0-336 (ug*h/ml)	AUC0-Infinity (ug*h/ml)	T1/2 (hr)	CL (ml/h)	Vd (mL/kg)
10D1F.Fc.A	25 mg/kg	217.686	6.000	28911.974	168078.210	639.672	0.037	34.093
10D1F.Fc.B	25 mg/kg	193.450	6.000	57007.087	228551.339	783.712	0.027	31.210

Figure 57B



Arms	Dose	Cmax (ug/ml)	Tmax (hr)	AUC0-336 (ug*h/ml)	AUC0-Infinity (ug*h/ml)	T1/2 (hr)	CL (ml/h)	Vd (mL/kg)
10D1F.Fc.A	100 mg/kg	250.516	6.000	69078.168	169396.299	438.789	0.148	93.857
10D1F.FcB	100 mg/kg	276.288	6.000	69125.006	108489.826	225.714	0.230	75.978

Figure 57C



Arms	Dose	Cmax (uB/ml)	Tmax (hr)	AUC0-336 (uB*h/ml)	AUC0-Infinity (ug*h/ml)	T1/2 (hr)	CL (ml/h)	Vd (mL/kg)
10D1F.Fc.A	250 mg/kg	297.919	6.000	81208.032	196765.343	440.240	0.318	200.826
10D1F.FcB	250 mg/kg	317.402	6.000	75091.243	141663.523	317.629	0.441	198.287

Figure 57D

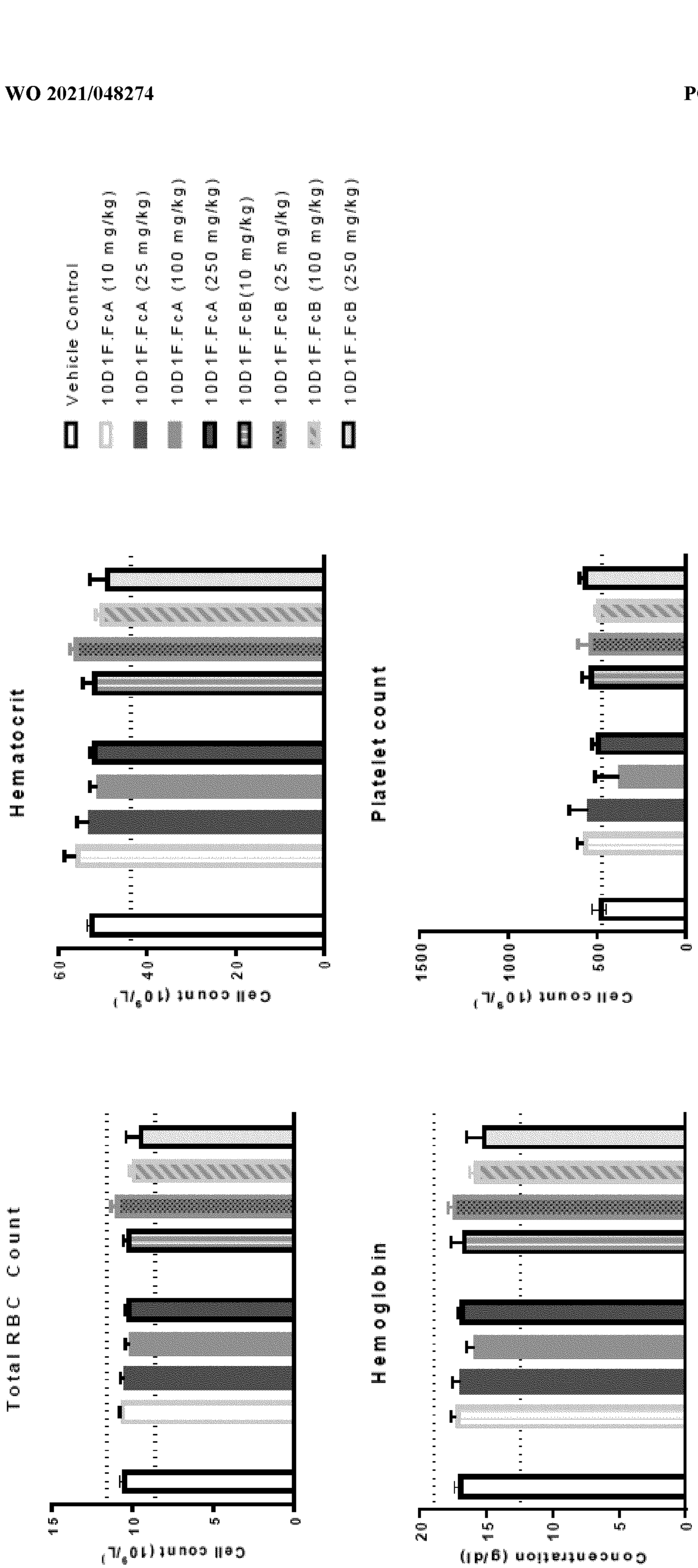

Vehicle Control
10D1F.FcA (10 mg/kg)
10D1F.FcA (25 mg/kg)
10D1F.FcA (100 mg/kg)
10D1F.FcA (250 mg/kg)
10D1F.FcB(10 mg/kg)
10D1F.FcB (25 mg/kg)
10D1F.FcB (100 mg/kg)
10D1F.FcB (250 mg/kg)
Hematocrit
Cell count (10⁹/L)
Platelet count
Cell count (10⁹/L)
Total RBC Count
Cell count (10⁹/L)
Hemoglobin
Concentration (g/dl)

Figure 58A

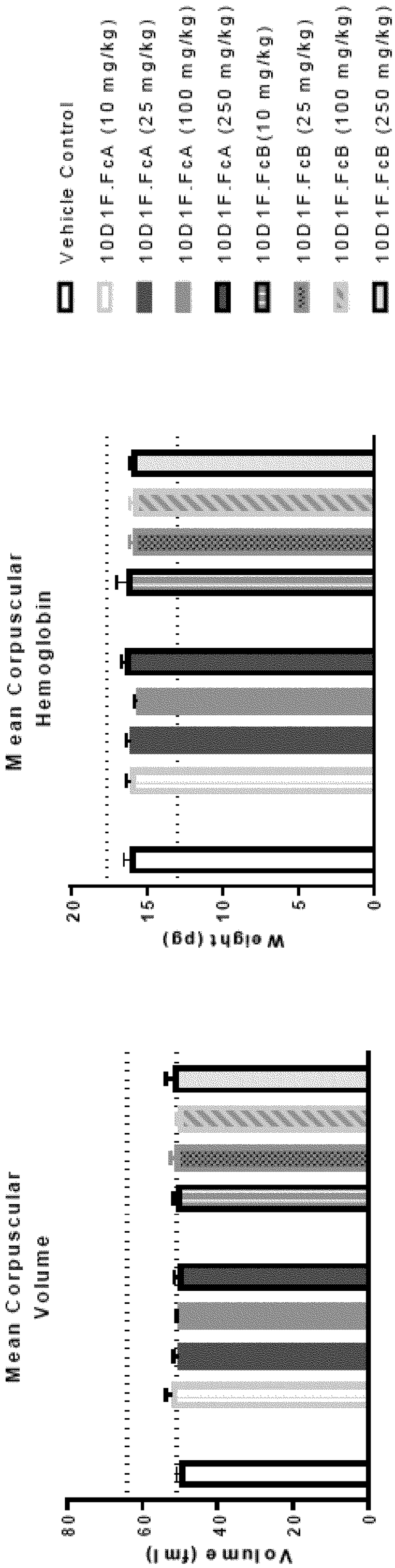

Vehicle Control
10D1F.FcA (10 mg/kg)
10D1F.FcA (25 mg/kg)
10D1F.FcA (100 mg/kg)
10D1F.FcA (250 mg/kg)
10D1F.FcB(10 mg/kg)
10D1F.FcB (25 mg/kg)
10D1F.FcB (100 mg/kg)
10D1F.FcB (250 mg/kg)
Mean Corpuscular Hemoglobin
W eight (pg)
0
5
10
15
20
Mean Corpuscular Volume
Volume (fm l)
0
20
40
60
80
Mean Corpuscular Hemoglobin Concentration
Concentration (g/dl)
0
10
20
30
40

Figure 58B

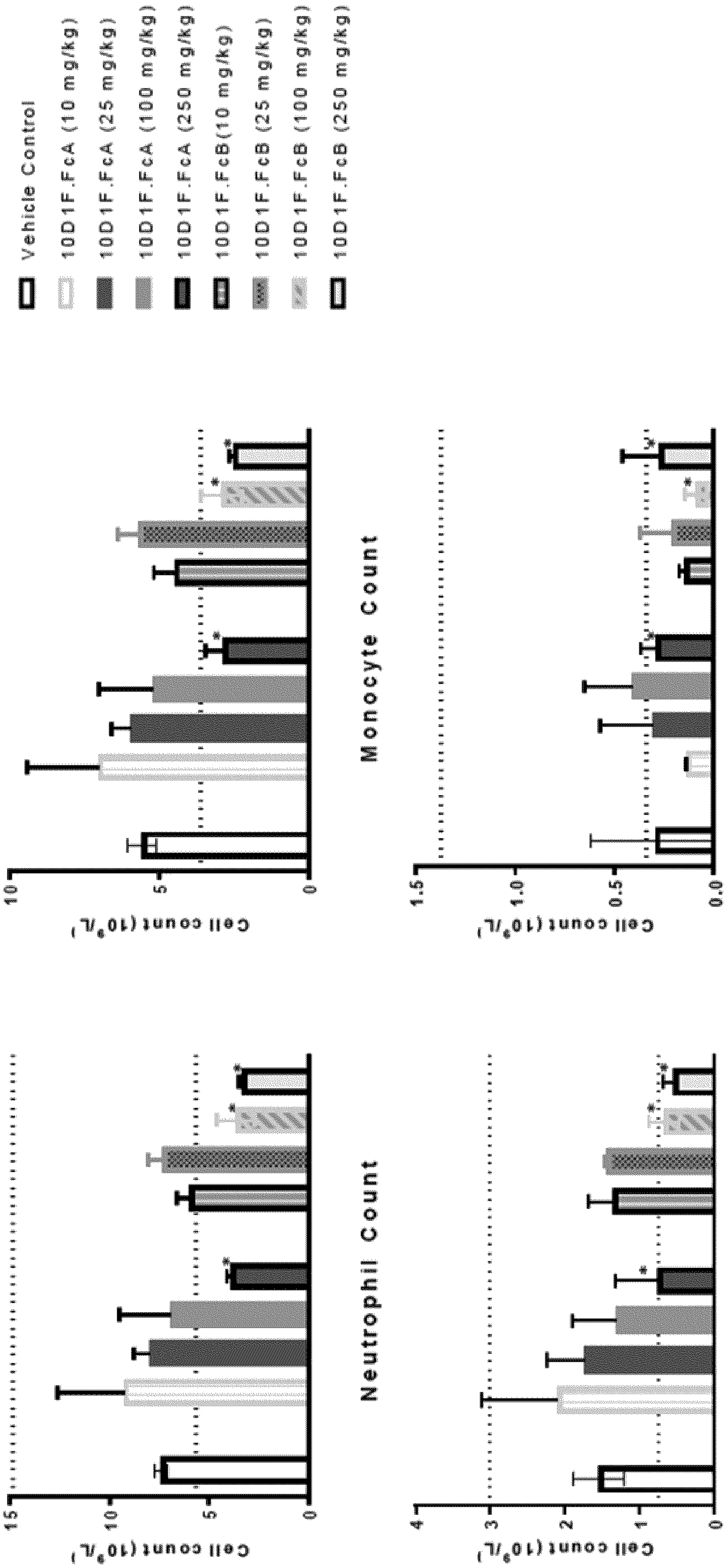

Vehicle Control
10D1F.FcA (10 mg/kg)
10D1F.FcA (25 mg/kg)
10D1F.FcA (100 mg/kg)
10D1F.FcA (250 mg/kg)
10D1F.FcB(10 mg/kg)
10D1F.FcB (25 mg/kg)
10D1F.FcB (100 mg/kg)
10D1F.FcB (250 mg/kg)
Lymphocyte Count
Monocyte Count
Total WBC Count
Neutrophil Count
Cell count (10^9/L)
0
5
10
0.0
0.5
1.0
1.5
0
1
2
3
4
0
5
10
15
*

Figure 58C

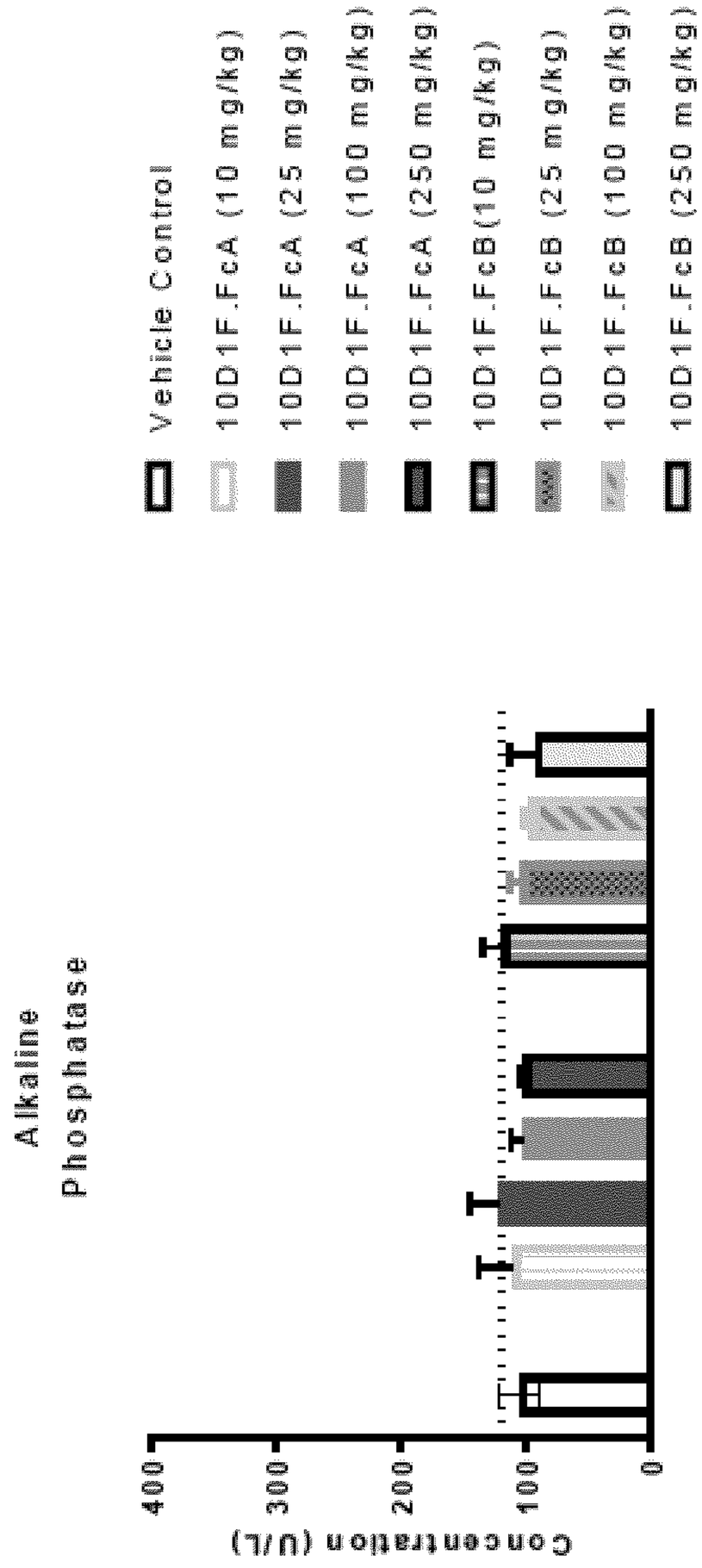

Vehicle Control
10D1F.FcA (10 mg/kg)
10D1F.FcA (25 mg/kg)
10D1F.FcA (100 mg/kg)
10D1F.FcA (250 mg/kg)
10D1F.FcB(10 mg/kg)
10D1F.FcB (25 mg/kg)
10D1F.FcB (100 mg/kg)
10D1F.FcB (250 mg/kg)
Alkaline Phosphatase
Concentration (U/L)
0
100
200
300
400
Total Protein
Concentration (g/dL)
0
2
4
6
8
10
Alanine Aminotransferase
Concentration (U/L)
0
50
100
150
Albumin
Concentration (g/dL)
0
1
2
3
4
5

Figure 58D

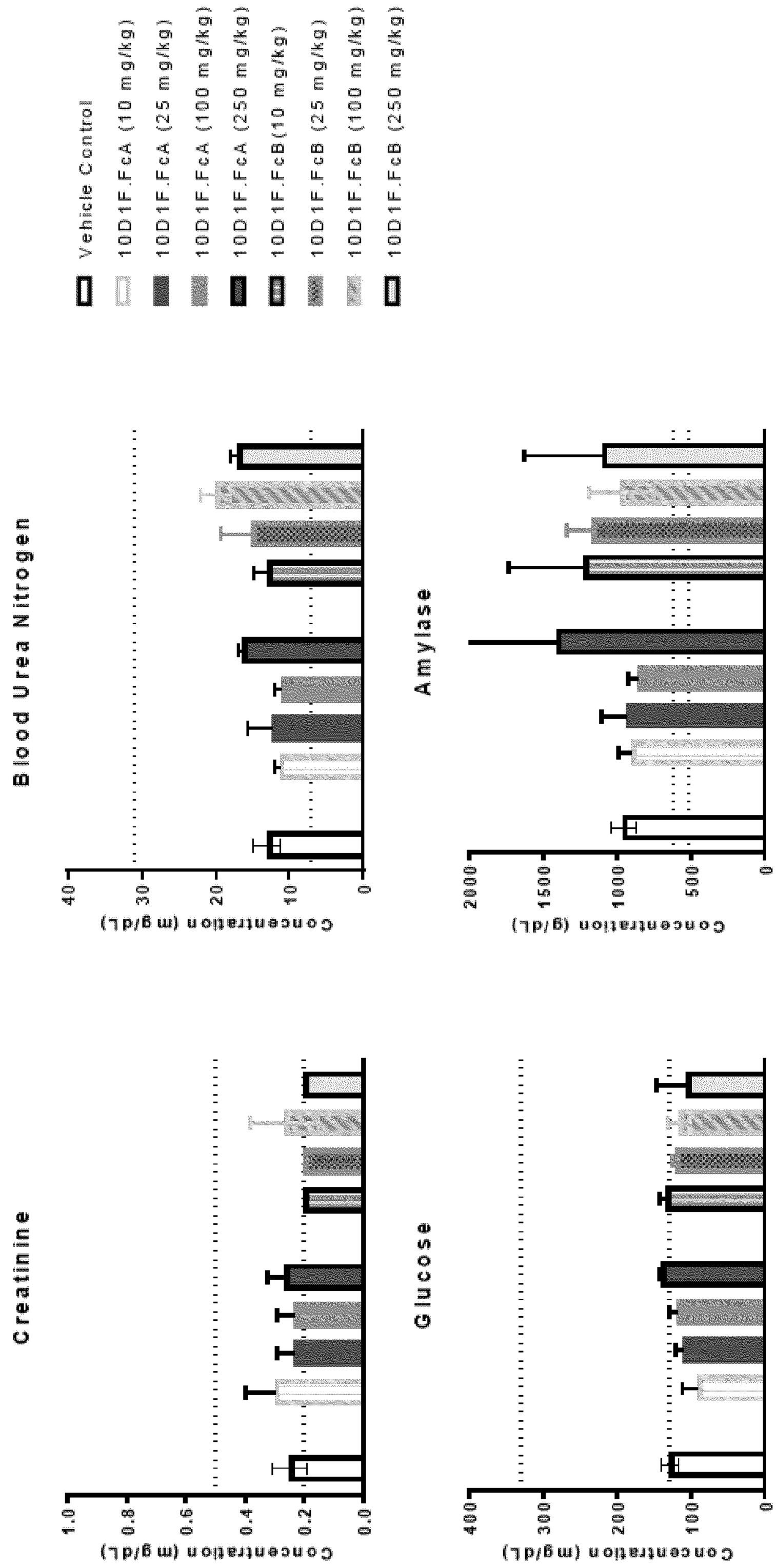

Vehicle Control
10D1F.FcA (10 mg/kg)
10D1F.FcA (25 mg/kg)
10D1F.FcA (100 mg/kg)
10D1F.FcA (250 mg/kg)
10D1F.FcB(10 mg/kg)
10D1F.FcB (25 mg/kg)
10D1F.FcB (100 mg/kg)
10D1F.FcB (250 mg/kg)
Blood Urea Nitrogen
Concentration (mg/dL)
0
10
20
30
40
Amylase
Concentration (g/dL)
0
500
1000
1500
2000
Creatinine
Concentration (mg/dL)
0.0
0.2
0.4
0.6
0.8
1.0
Glucose
Concentration (mg/dL)
0
100
200
300
400

Figure 58E

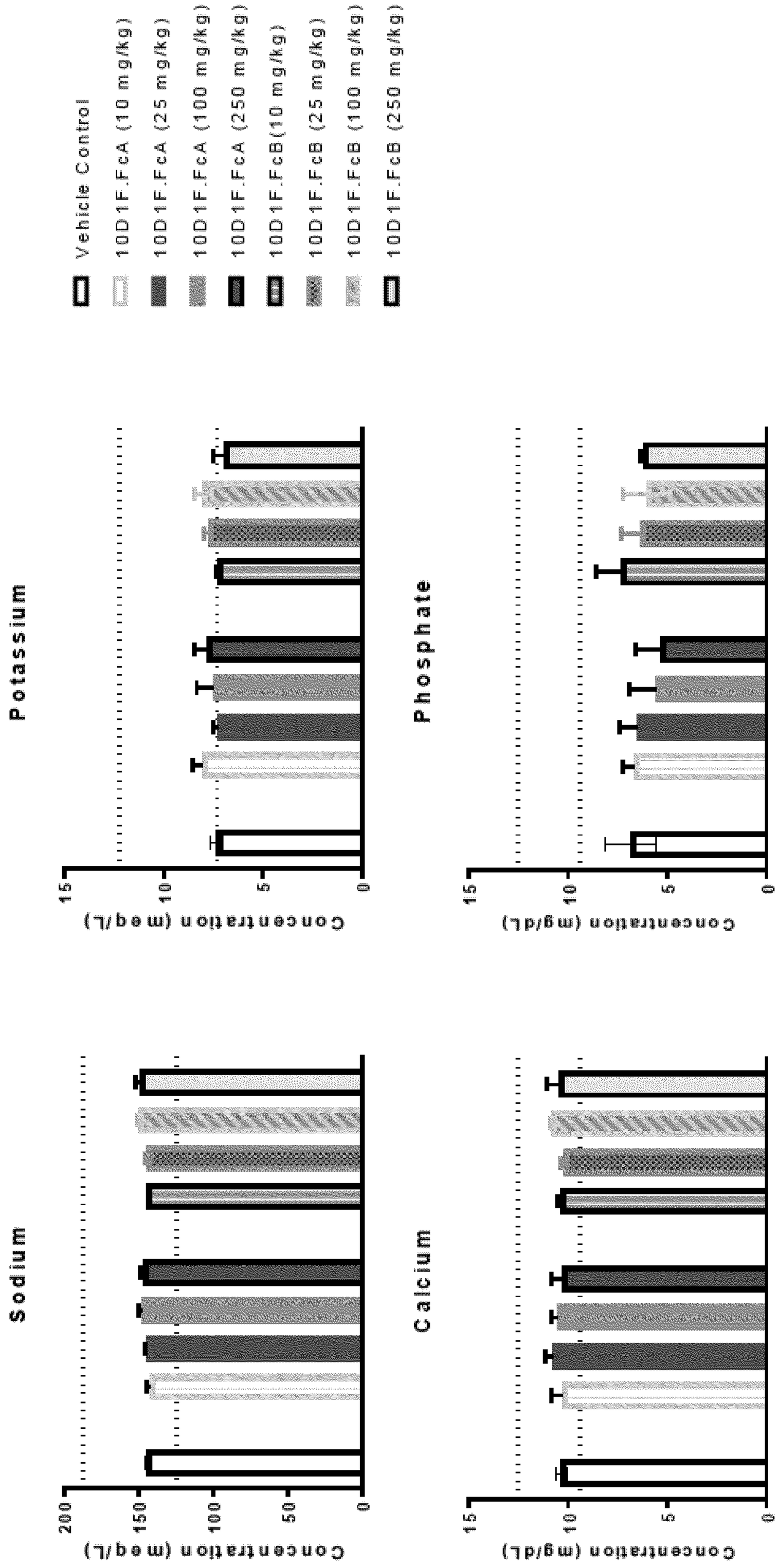

Vehicle Control
10D1F.FcA (10 mg/kg)
10D1F.FcA (25 mg/kg)
10D1F.FcA (100 mg/kg)
10D1F.FcA (250 mg/kg)
10D1F.FcB(10 mg/kg)
10D1F.FcB (25 mg/kg)
10D1F.FcB (100 mg/kg)
10D1F.FcB (250 mg/kg)
Potassium
Phosphate
Sodium
Calcium
Concentration (meq/L)
Concentration (mg/dL)
0
5
10
15
50
100
150
200

Figure 58F

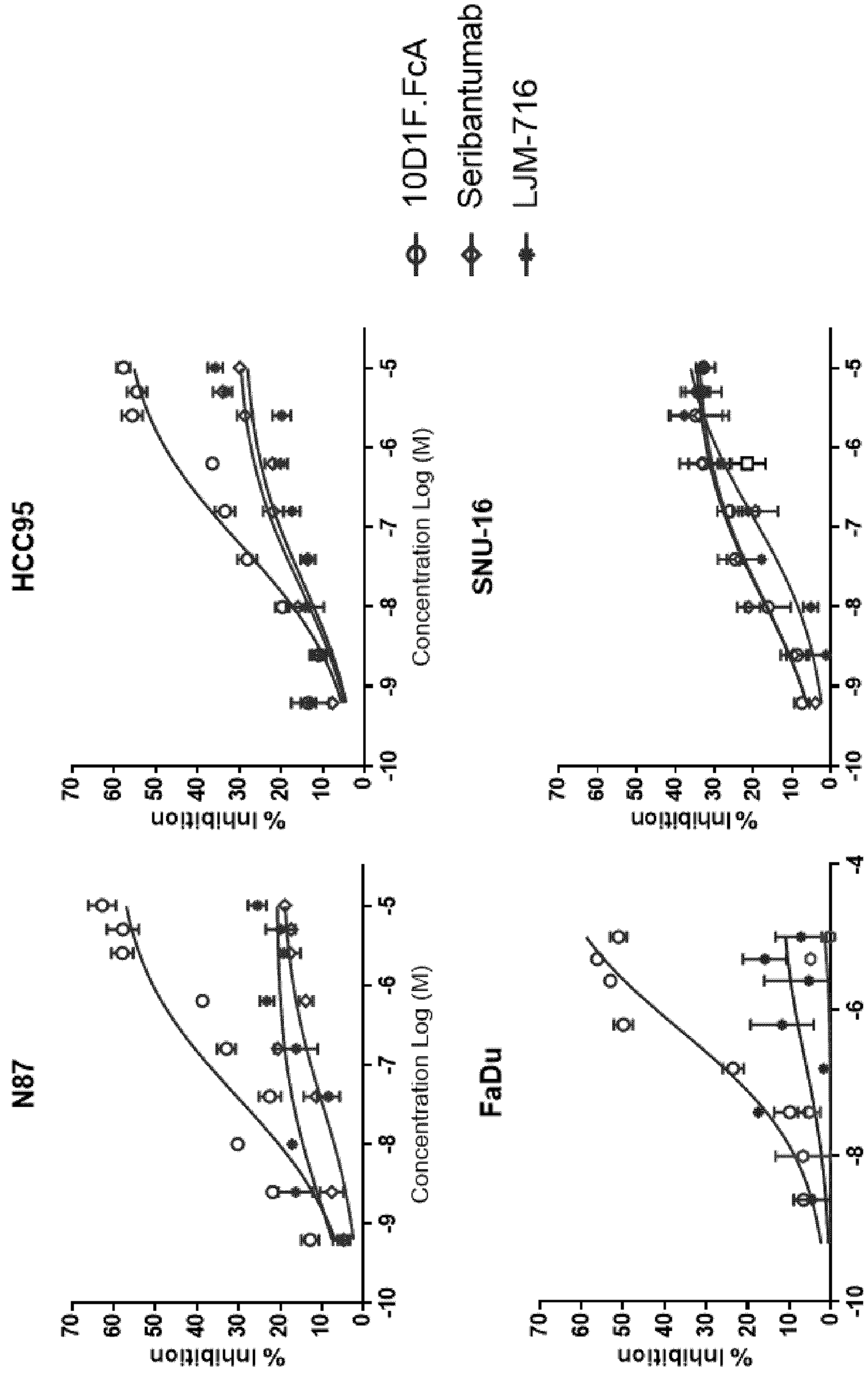

10D1F.FcA
Seribantumab
LJM-716
HCC95
SNU-16
N87
FaDu
% Inhibition
Concentration Log (M)
0
10
20
30
40
50
60
70
-10
-9
-8
-7
-6
-5
-4

Figure 59A

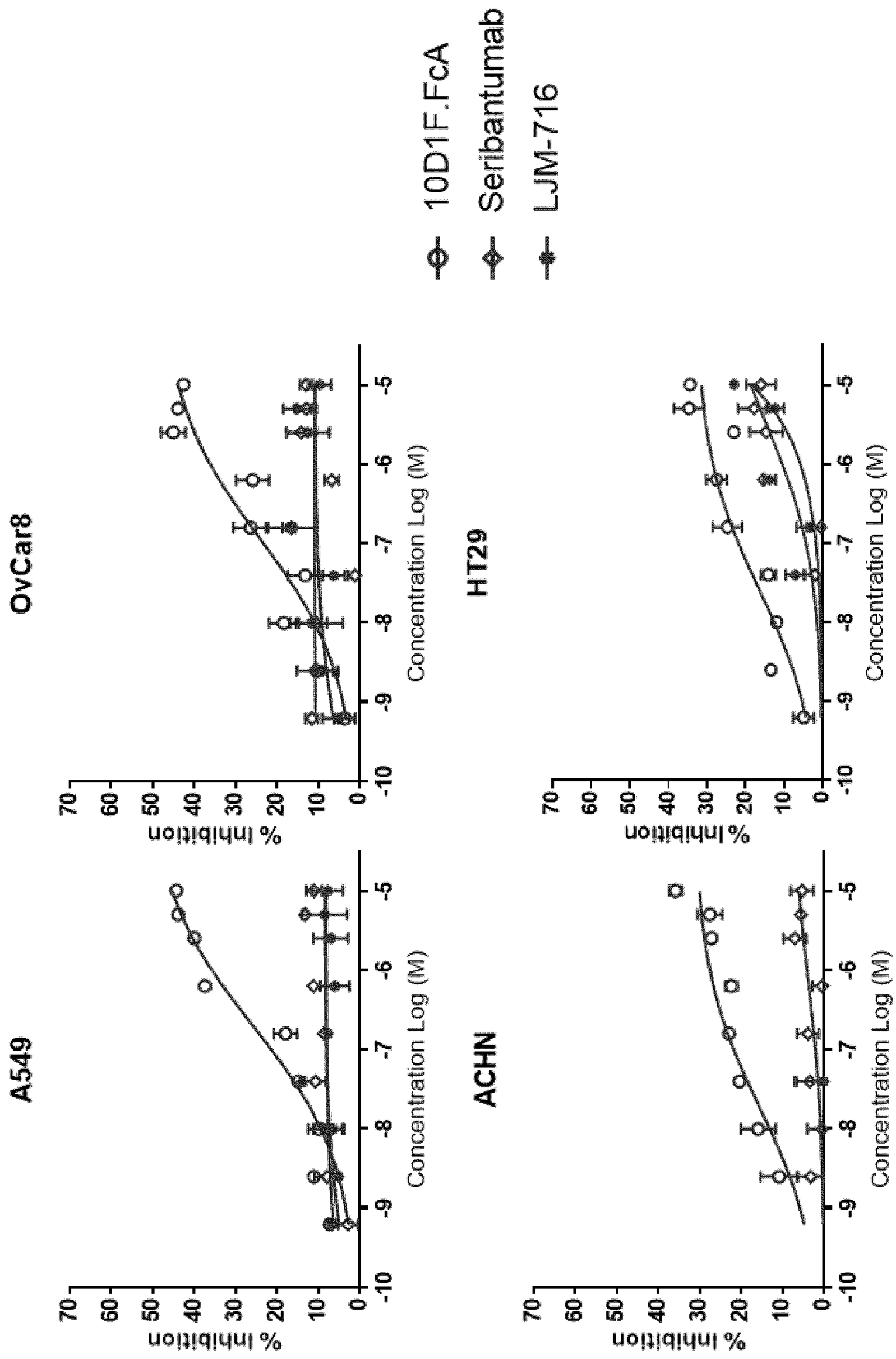

10D1F.FcA
Seribantumab
LJM-716
OvCar8
HT29
A549
ACHN
% Inhibition
Concentration Log (M)
70
60
50
40
30
20
10
0
-5
-6
-7
-8
-9
-10

Figure 59B

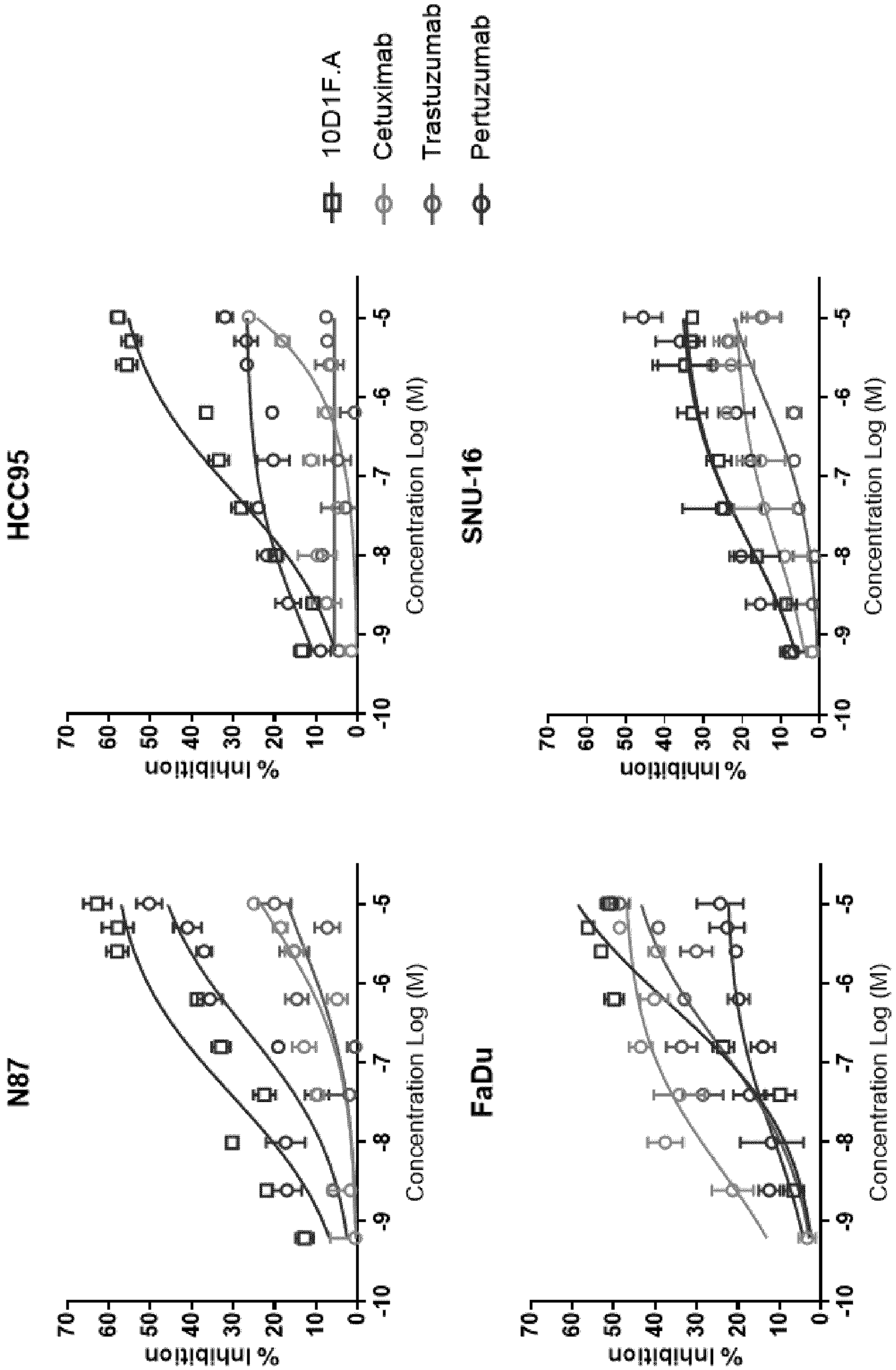

10D1F.A
Cetuximab
Trastuzumab
Pertuzumab
HCC95
SNU-16
N87
FaDu
% Inhibition
Concentration Log (M)
70
60
50
40
30
20
10
0
-5
-6
-7
-8
-9
-10

Figure 59C

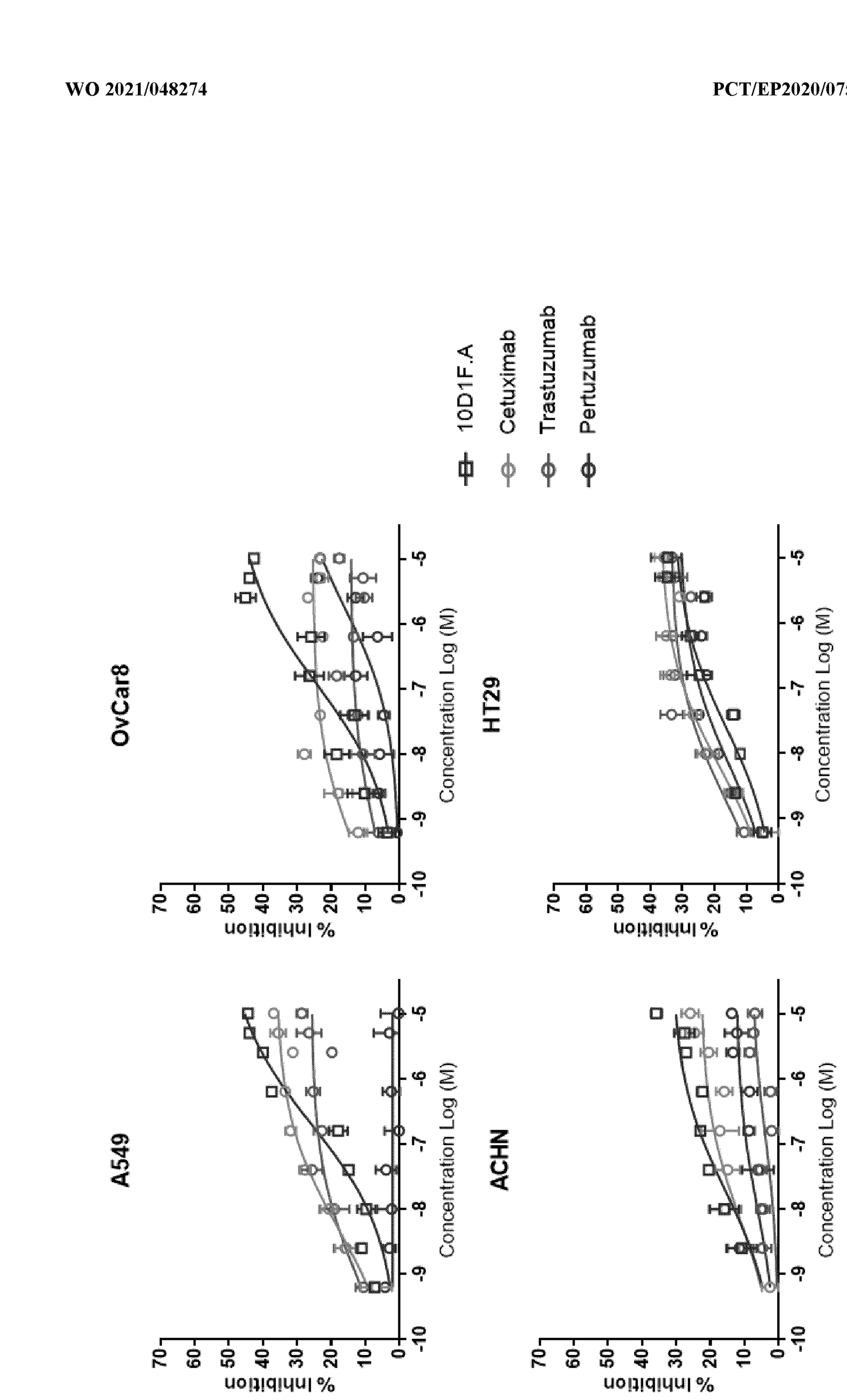

10D1F.A
Cetuximab
Trastuzumab
Pertuzumab
OvCar8
HT29
A549
ACHN
% Inhibition
Concentration Log (M)
-10
-9
-8
-7
-6
-5
0
10
20
30
40
50
60
70

Figure 59D

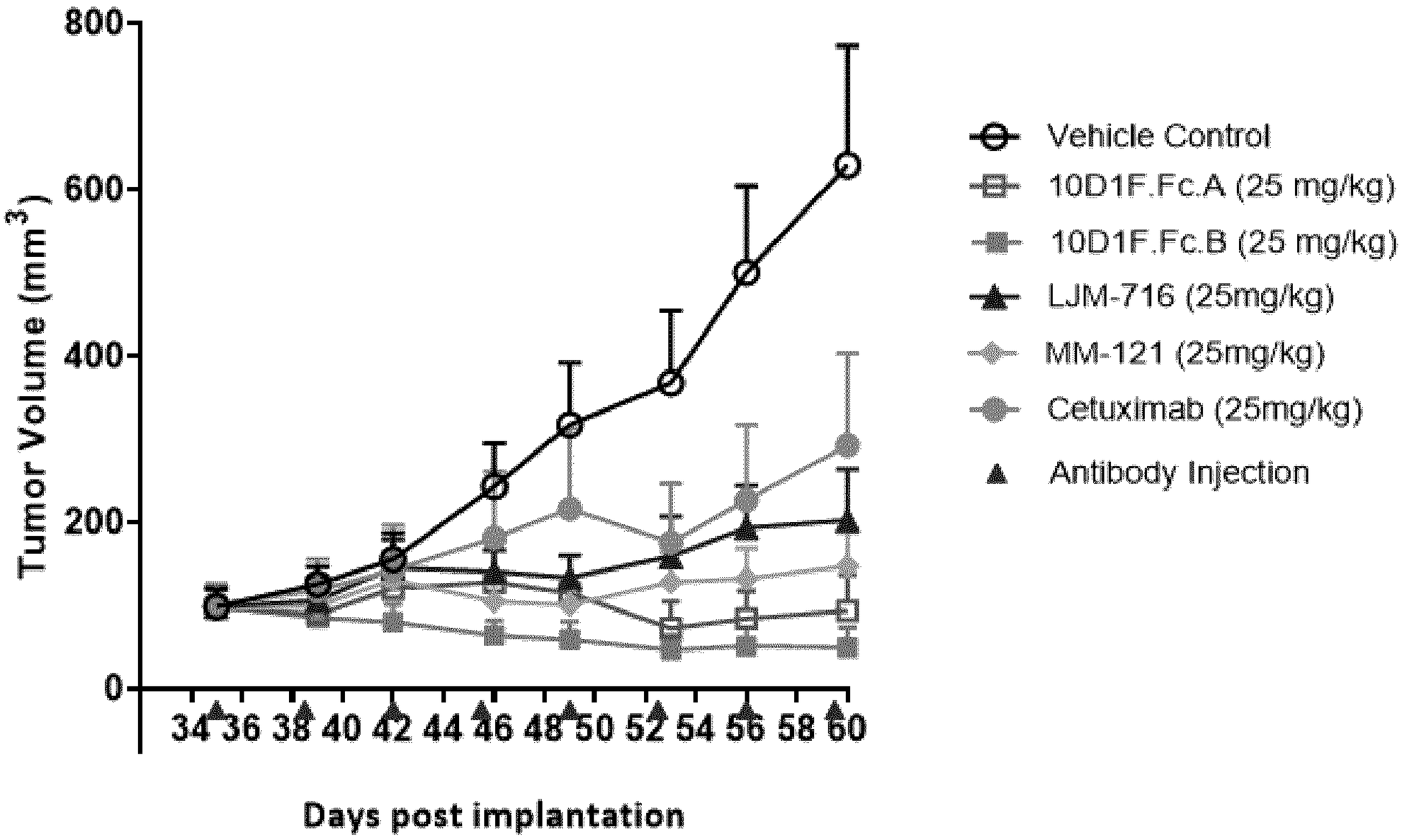


Figure 60

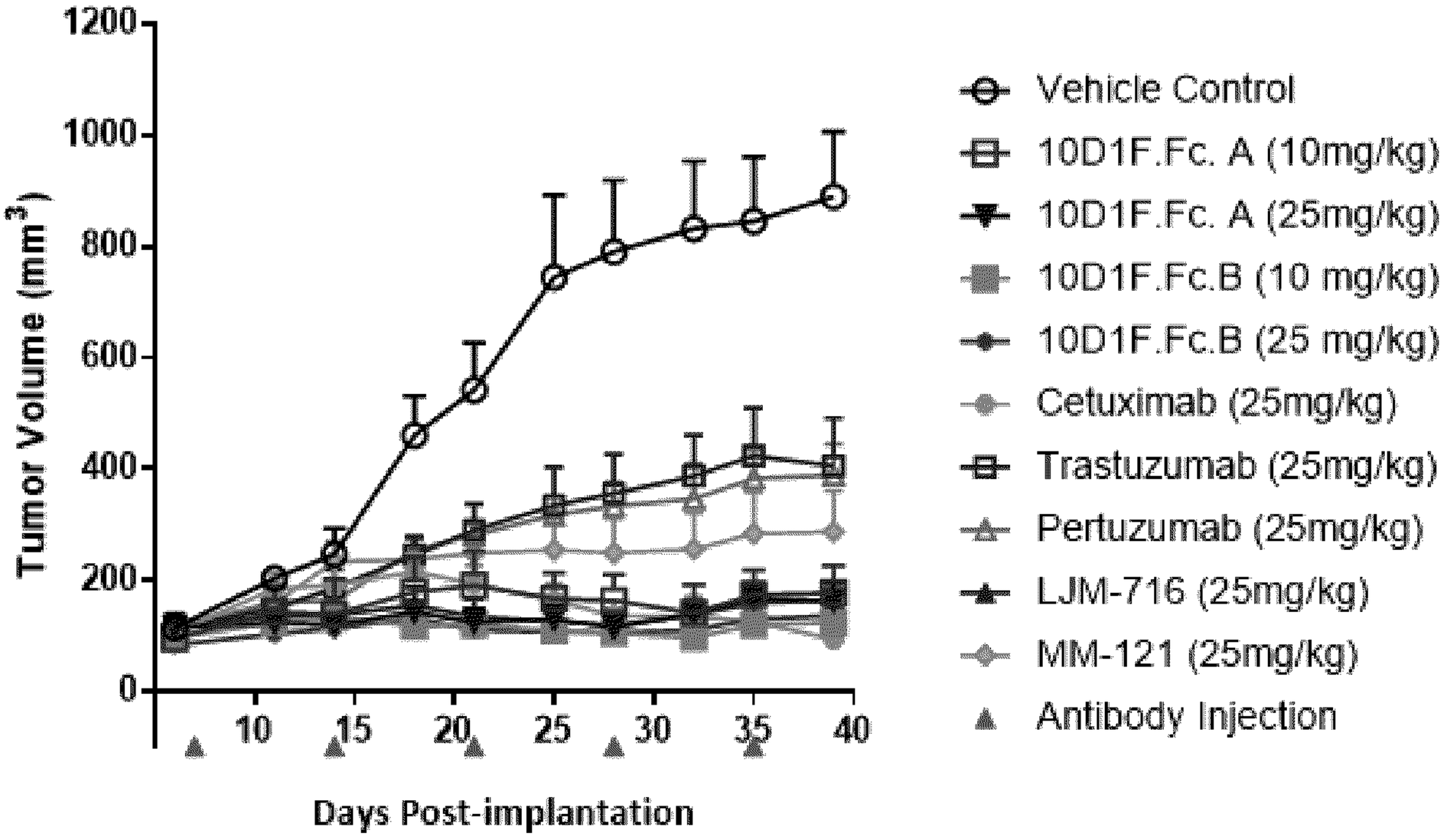


Figure 61

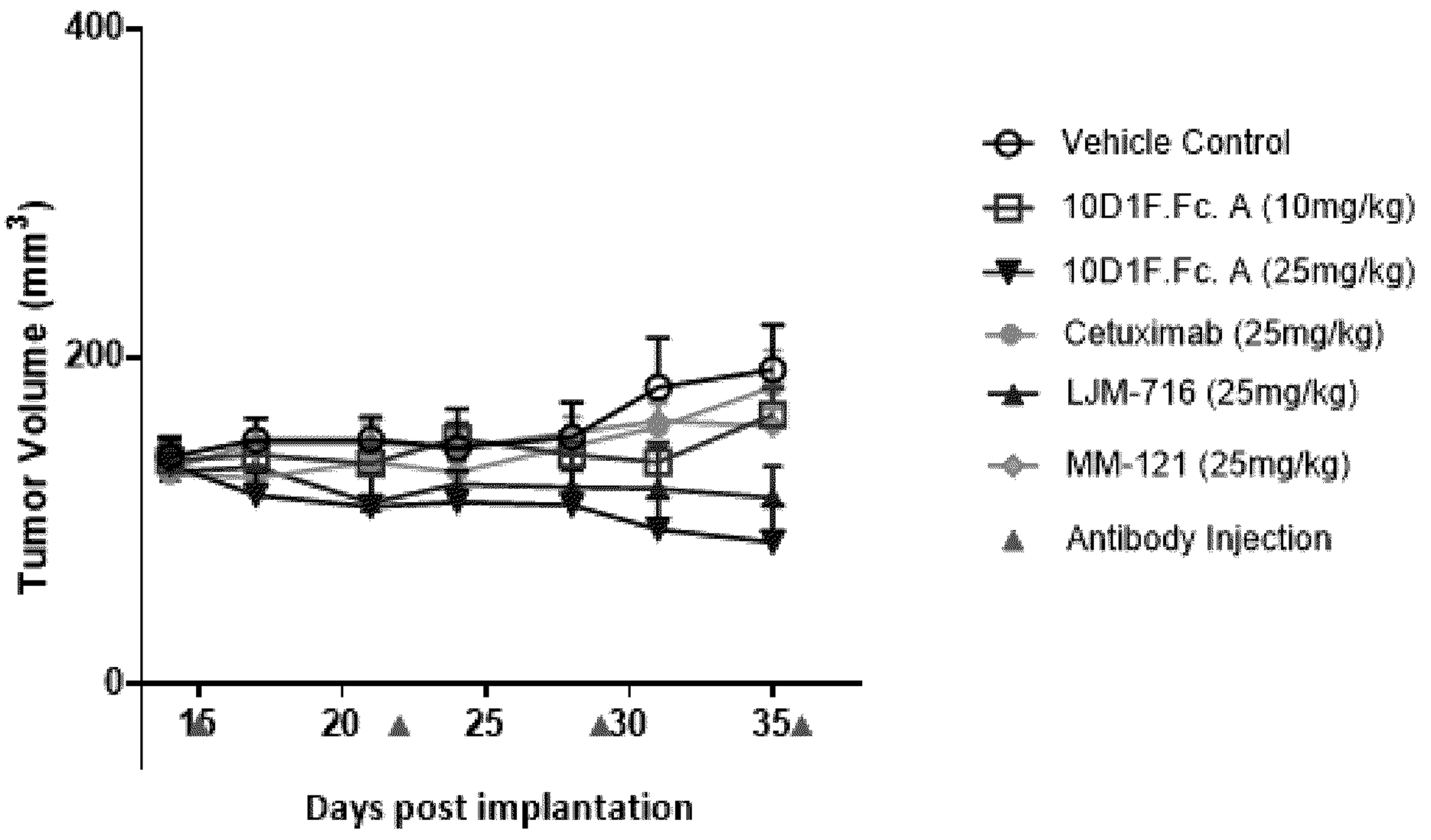


Figure 62

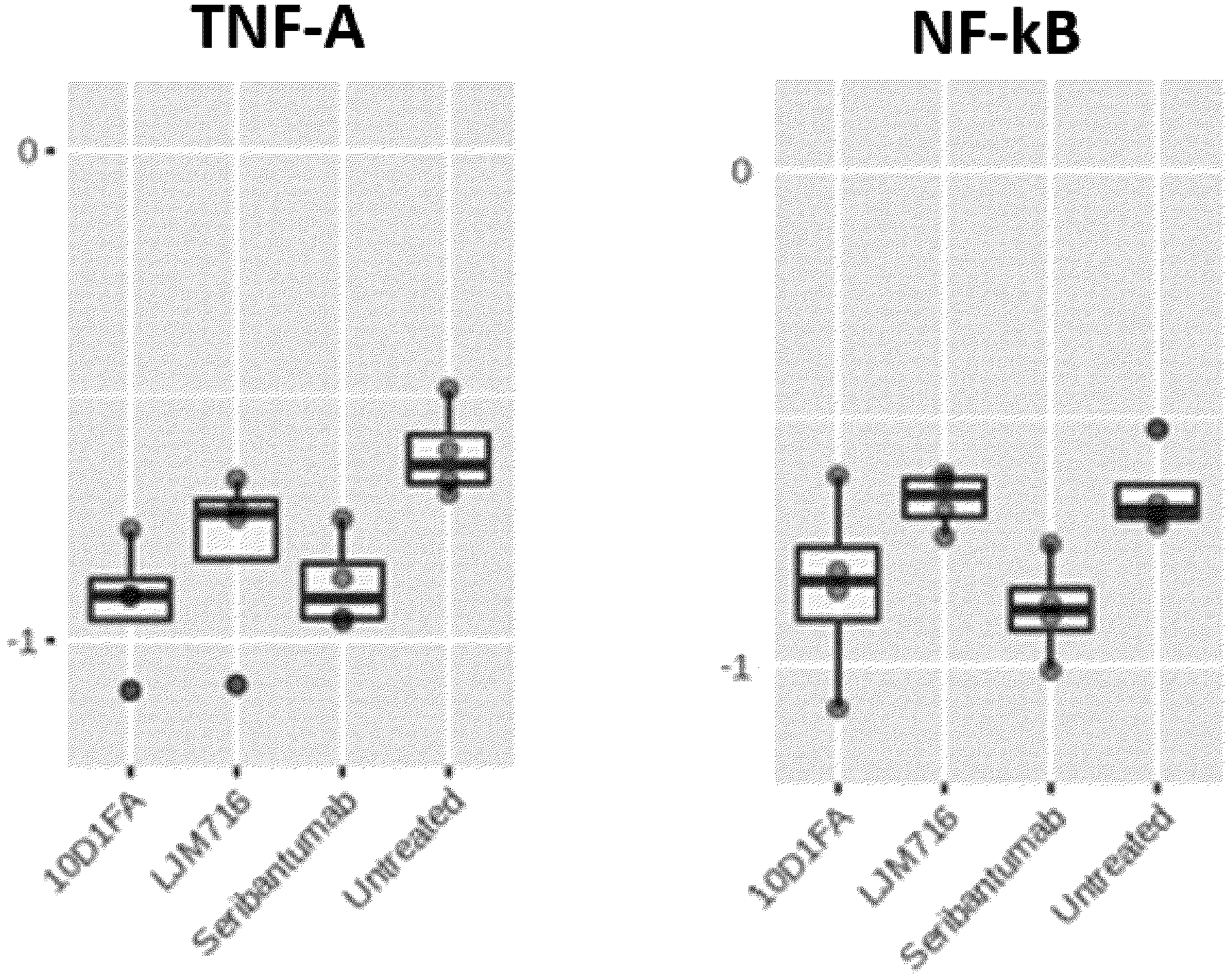


Figure 63A

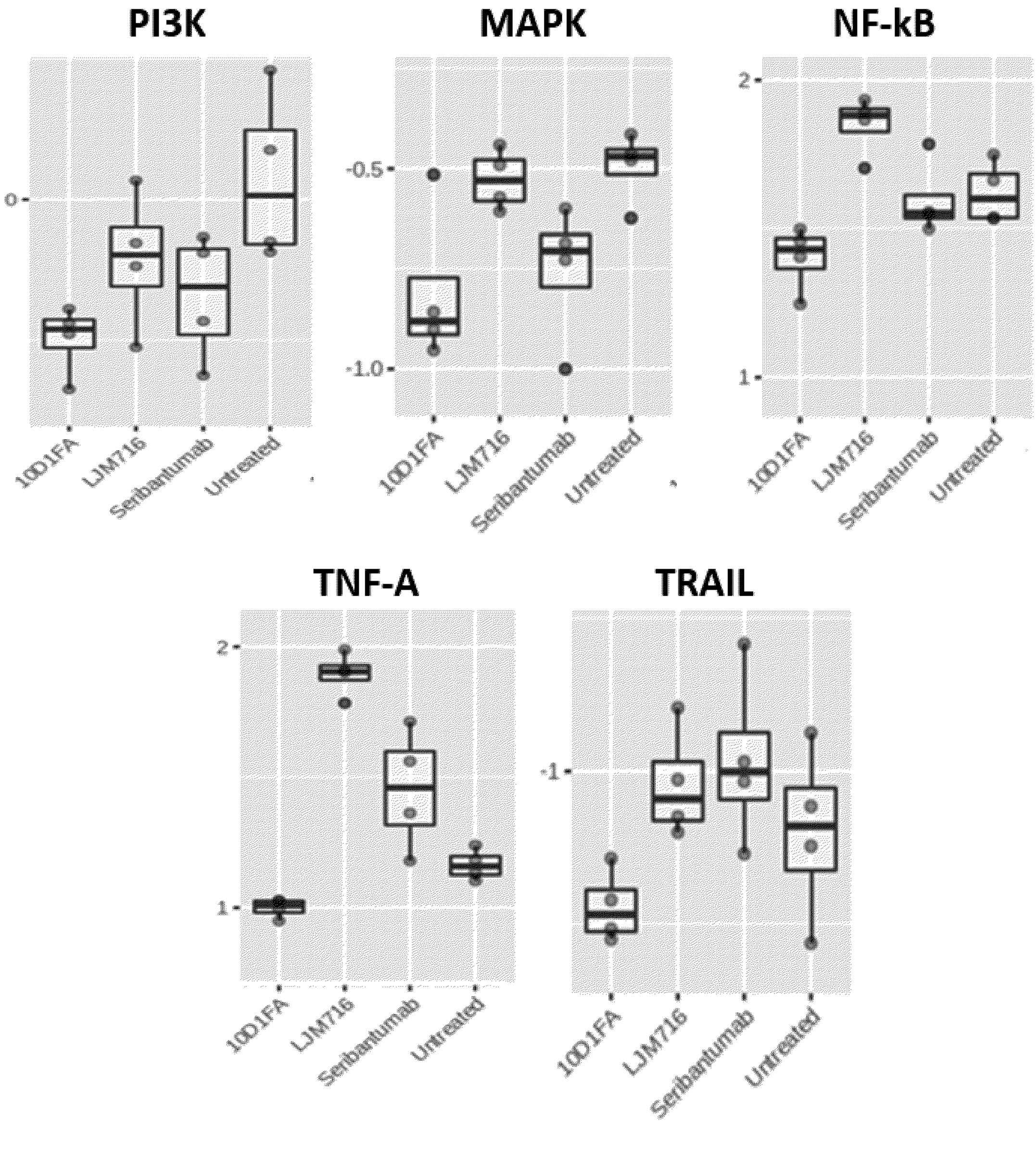

PI3K
0
10D1FA
LJM716
Seribantumab
Untreated
MAPK
-0.5
-1.0
10D1FA
LJM716
Seribantumab
Untreated
NF-kB
2
1
10D1FA
LJM716
Seribantumab
Untreated
TNF-A
2
1
10D1FA
LJM716
Seribantumab
Untreated
TRAIL
1
-1
10D1FA
LJM716
Seribantumab
Untreated

Figure 63B

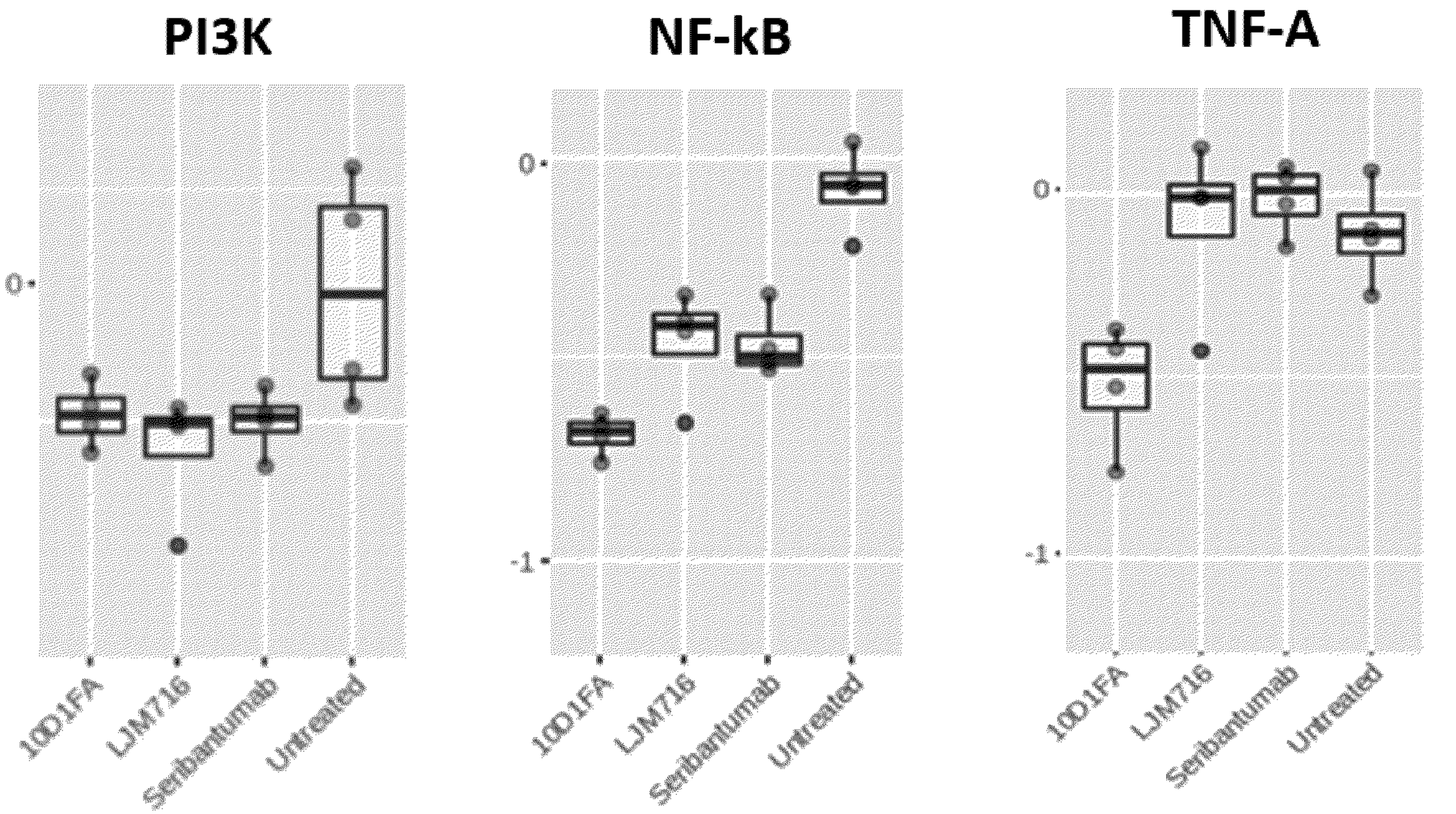
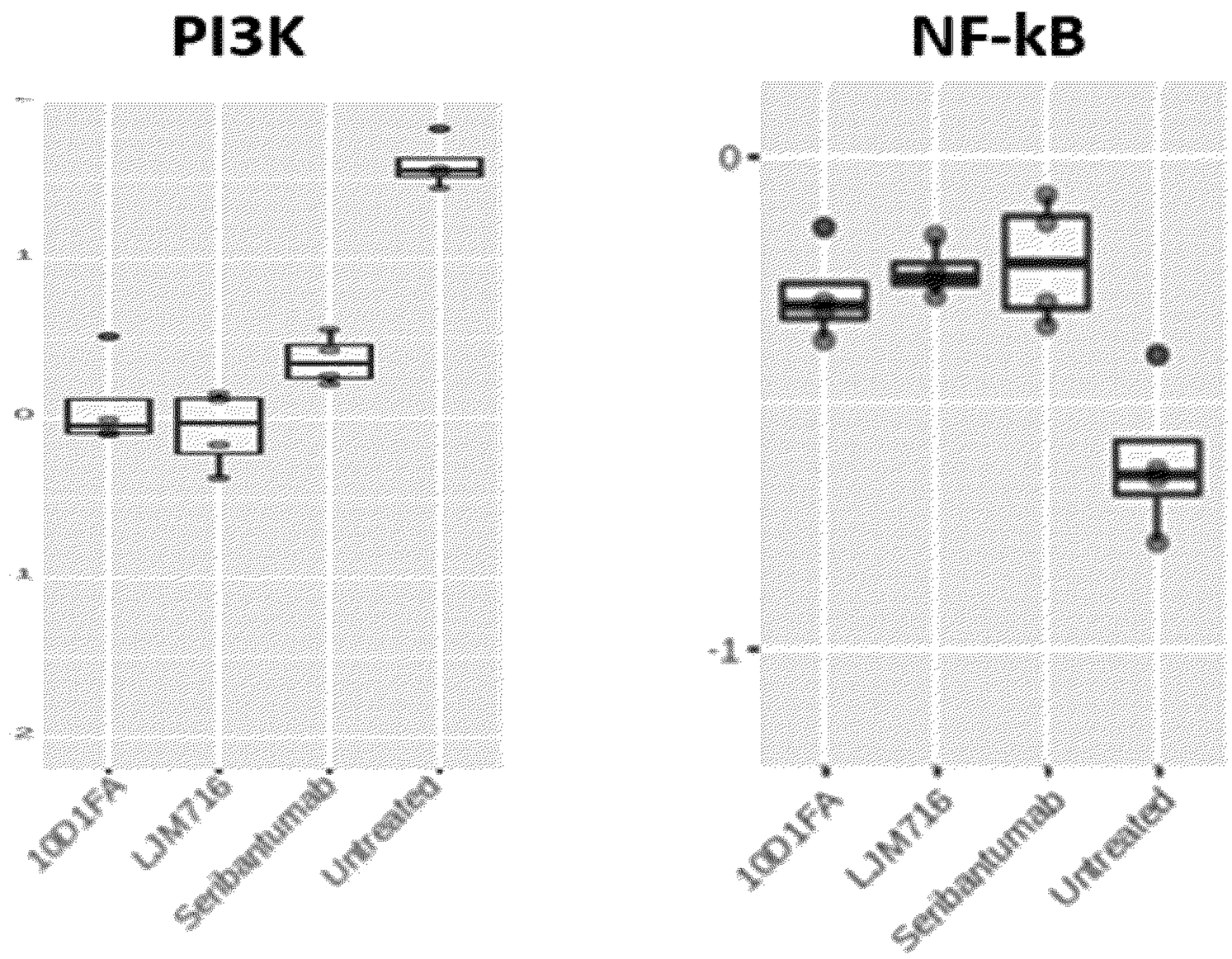
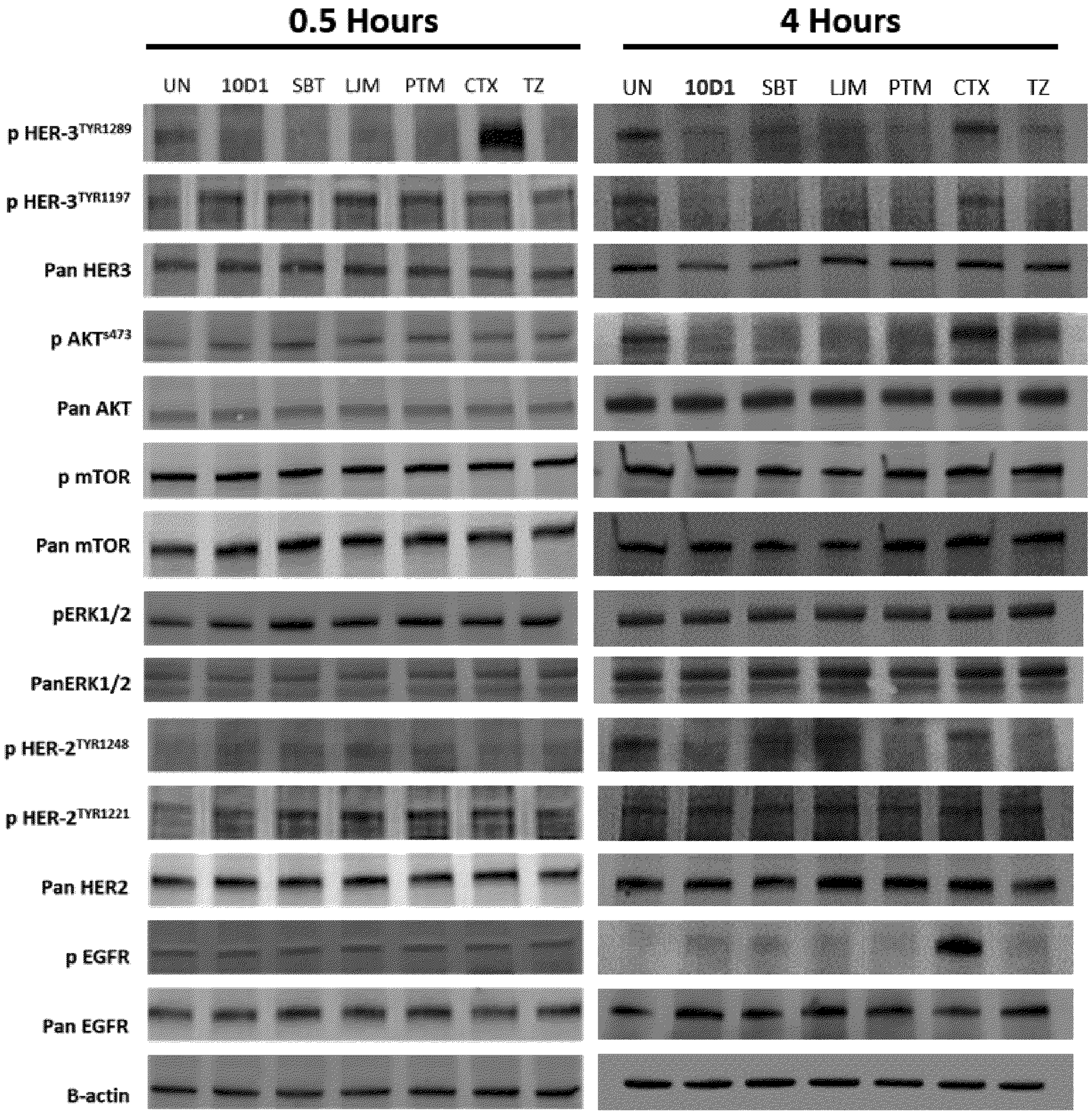


Figure 63C



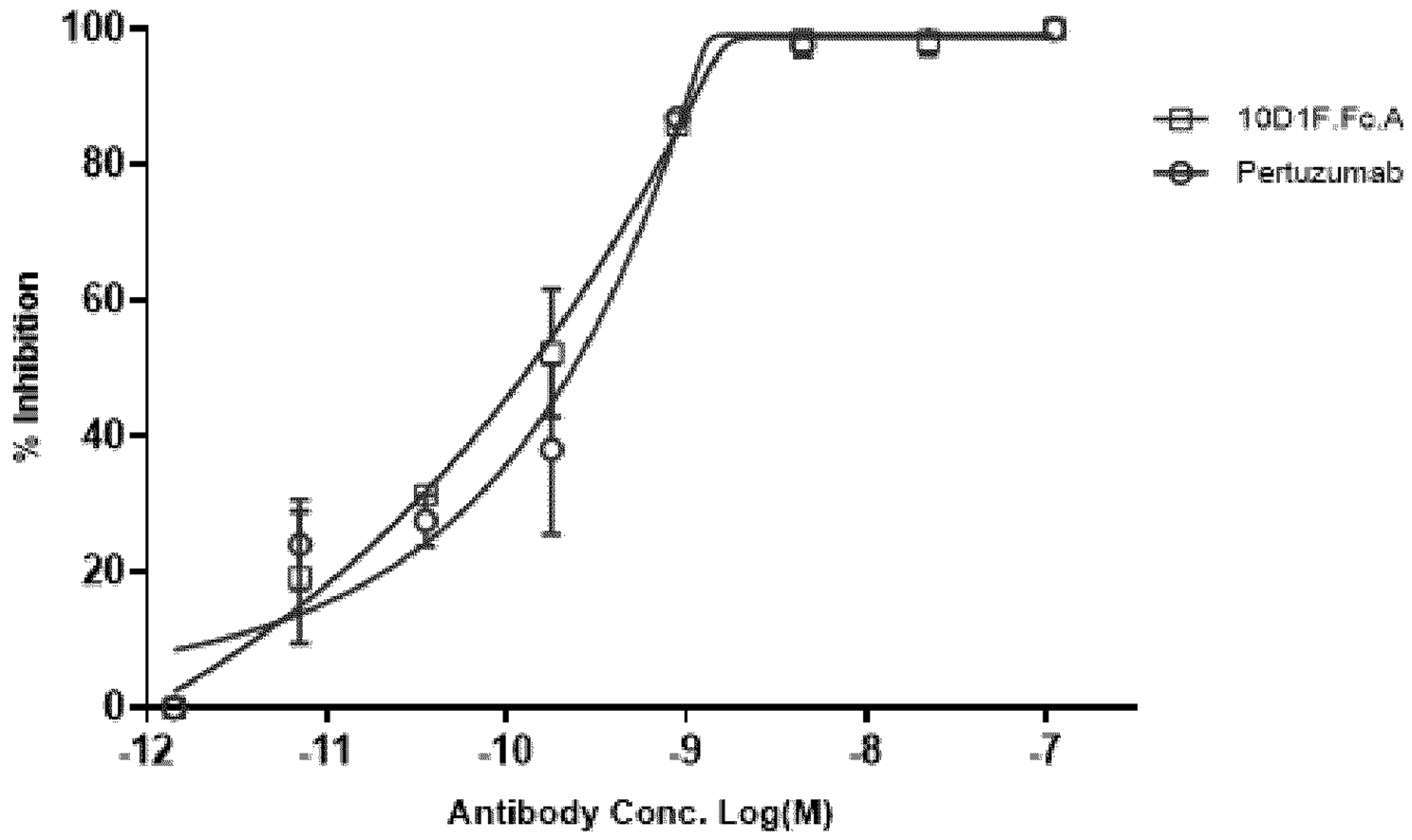
s

Figure 63D



Legend:
UN = Untreated
10D1 = 10D1F.A
SBT = Seribantumab (MM-121)
LIM = Elgemtumab (LIM-716)
PTM = Pertuzumab
CTX = Cetuximab

Figure 64



	10D1F.FcA	Pertuzumab	Isotype
IC_{50} (M)	3.715e-011	2.481e-010	NA

Figure 65

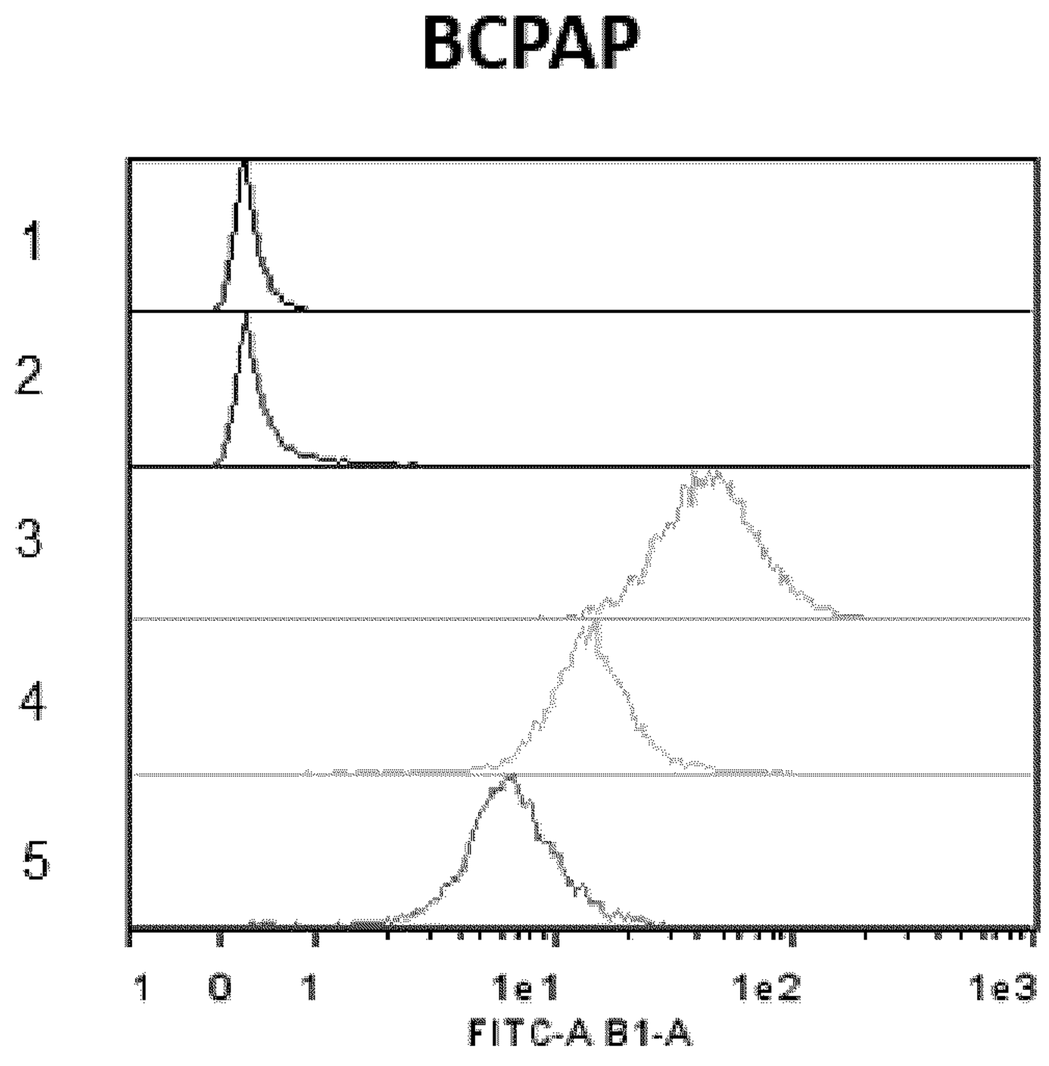


Figure 66A

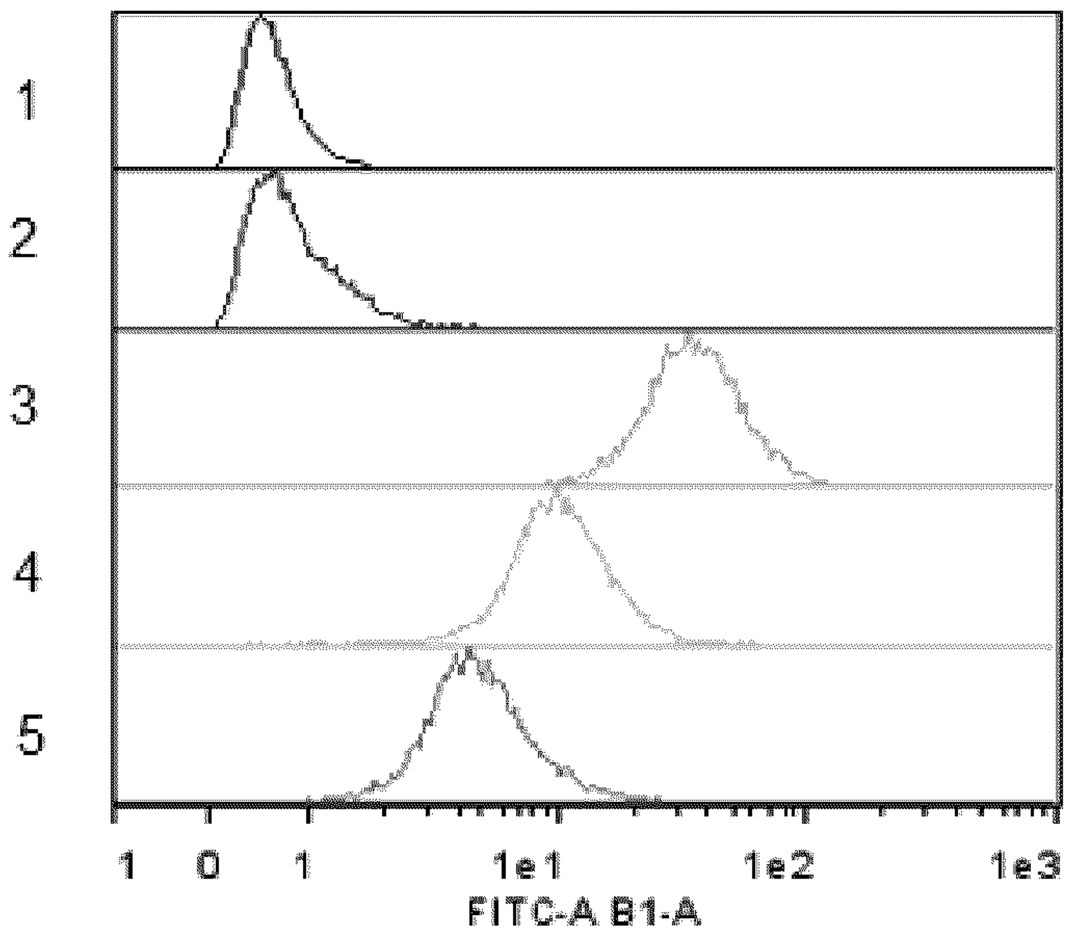


Figure 66B

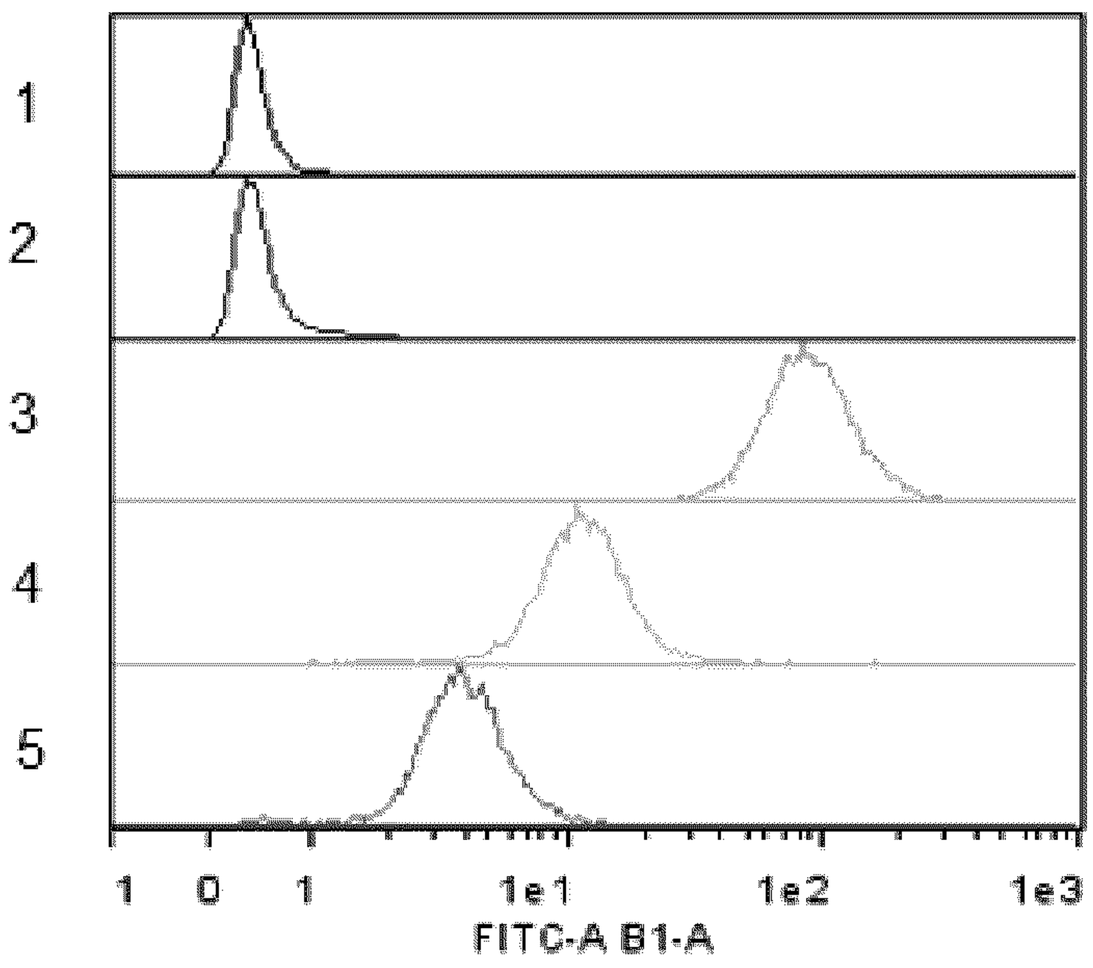


Figure 66C

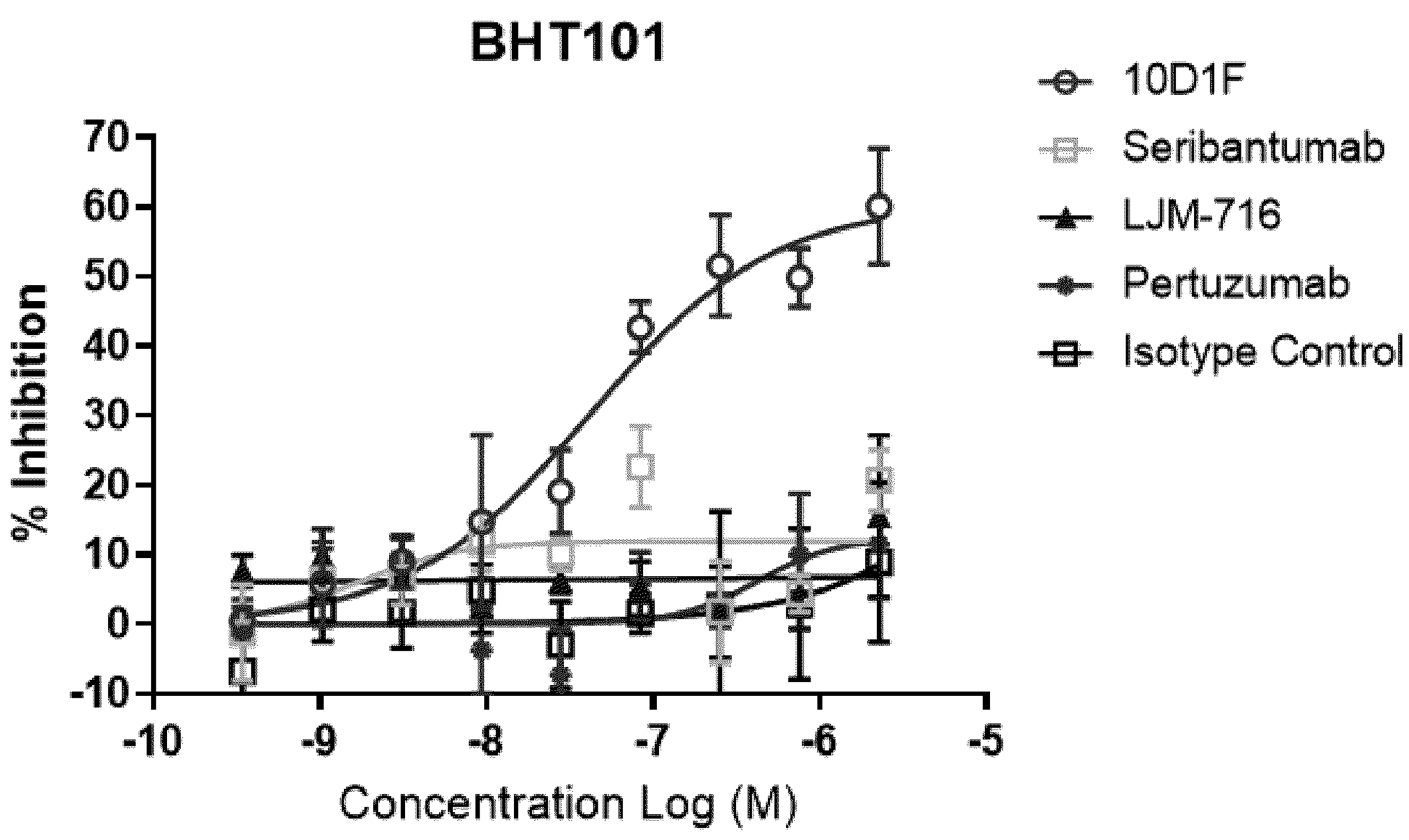


Figure 67A

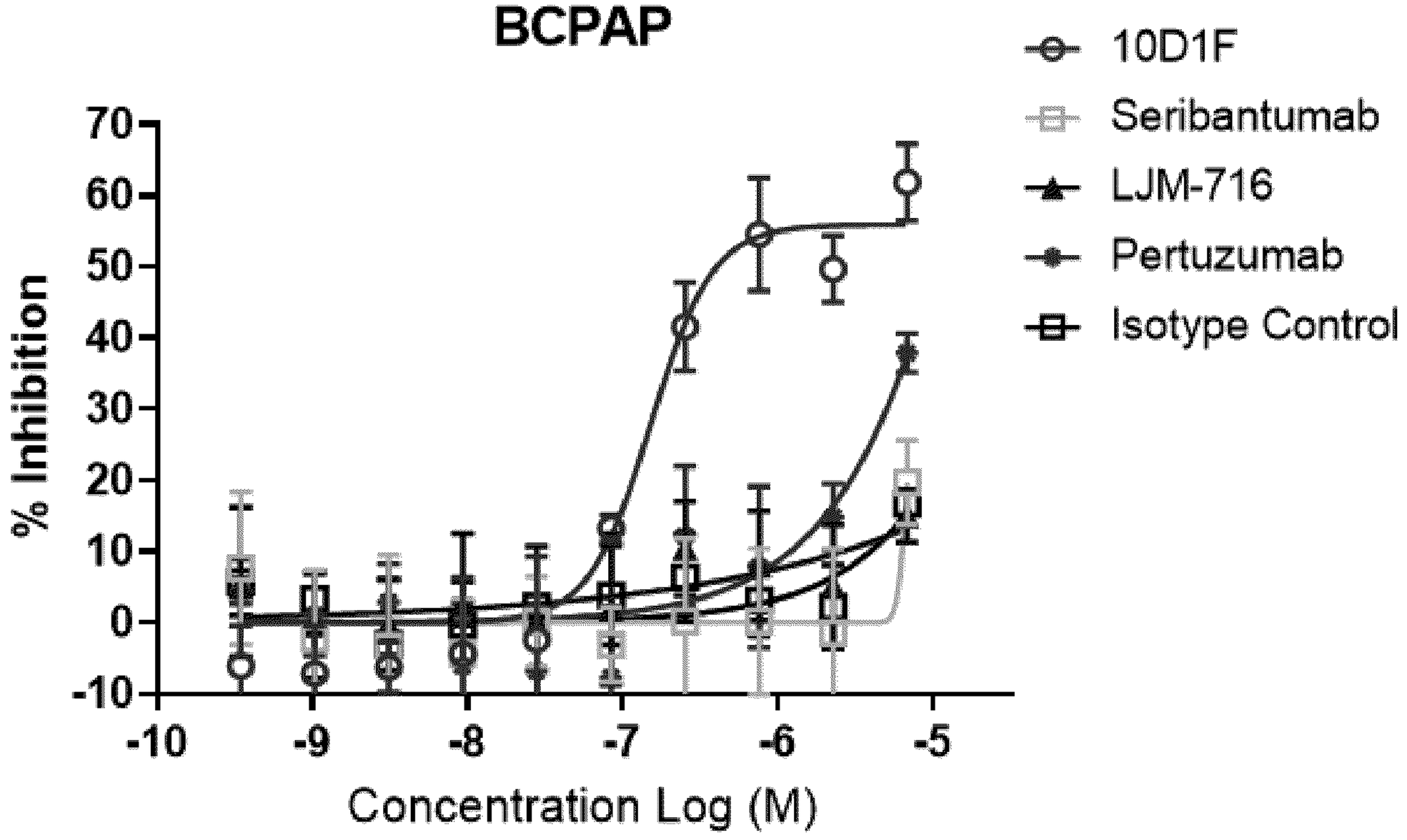


Figure 67B

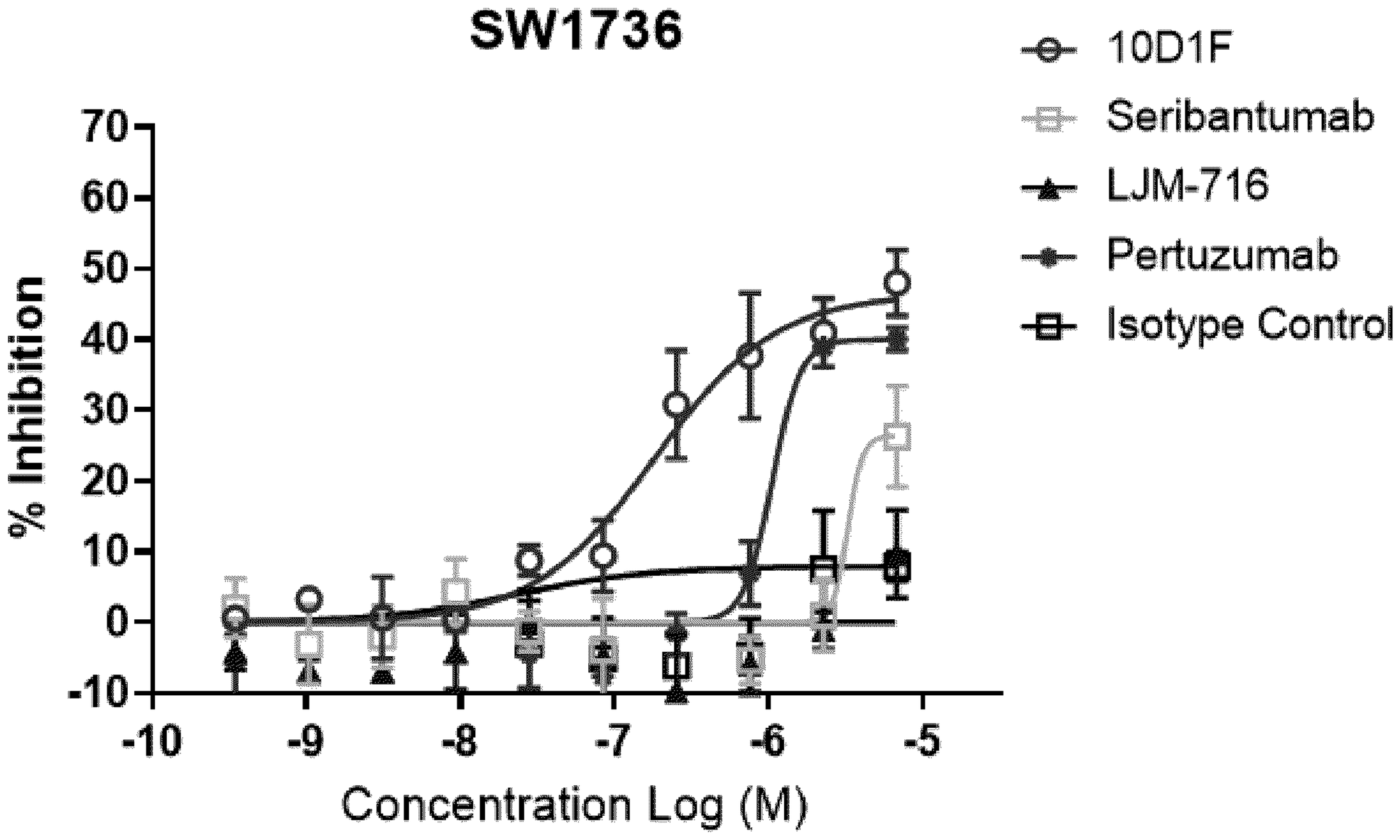


Figure 67C

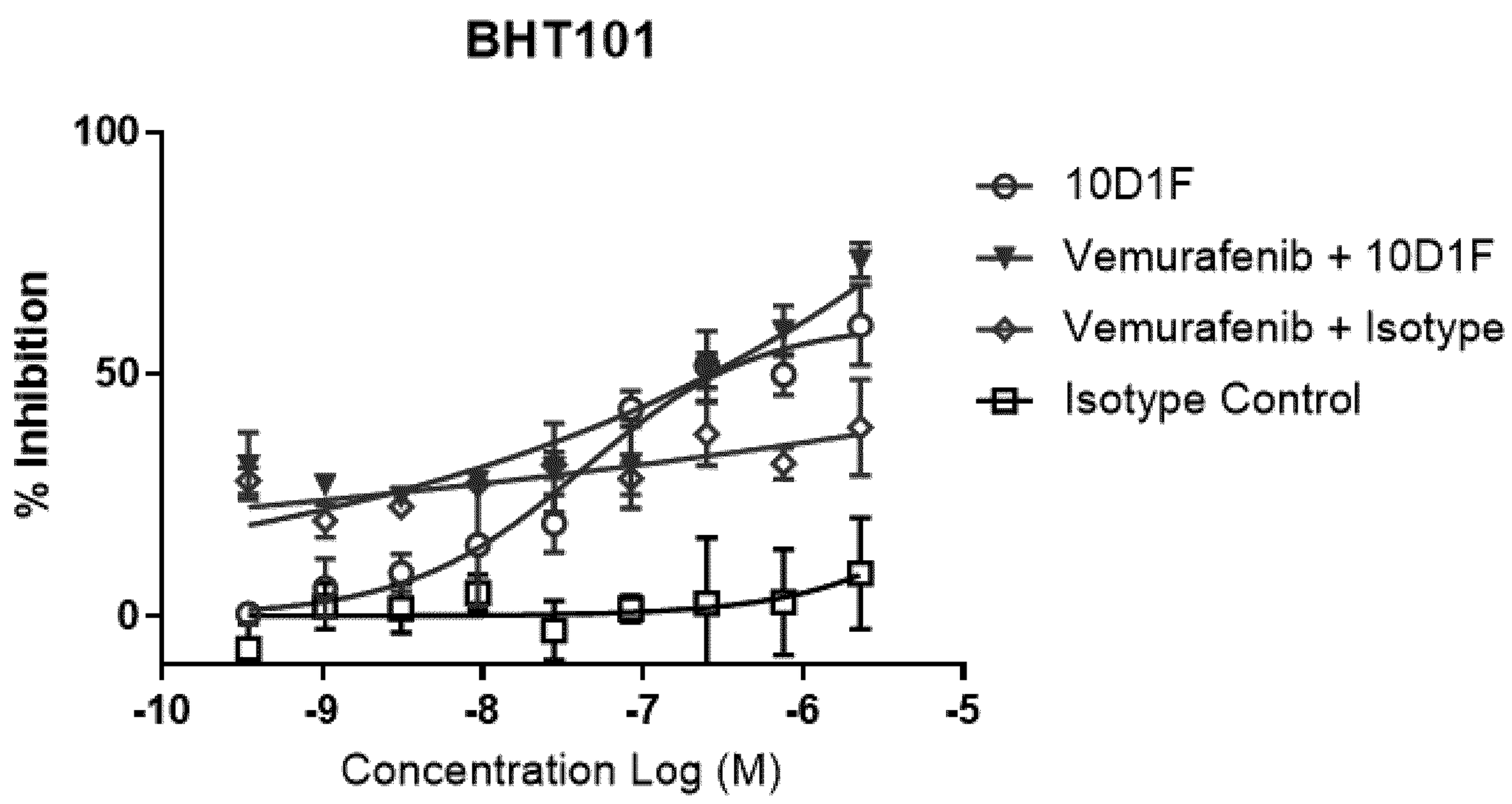


Figure 68A

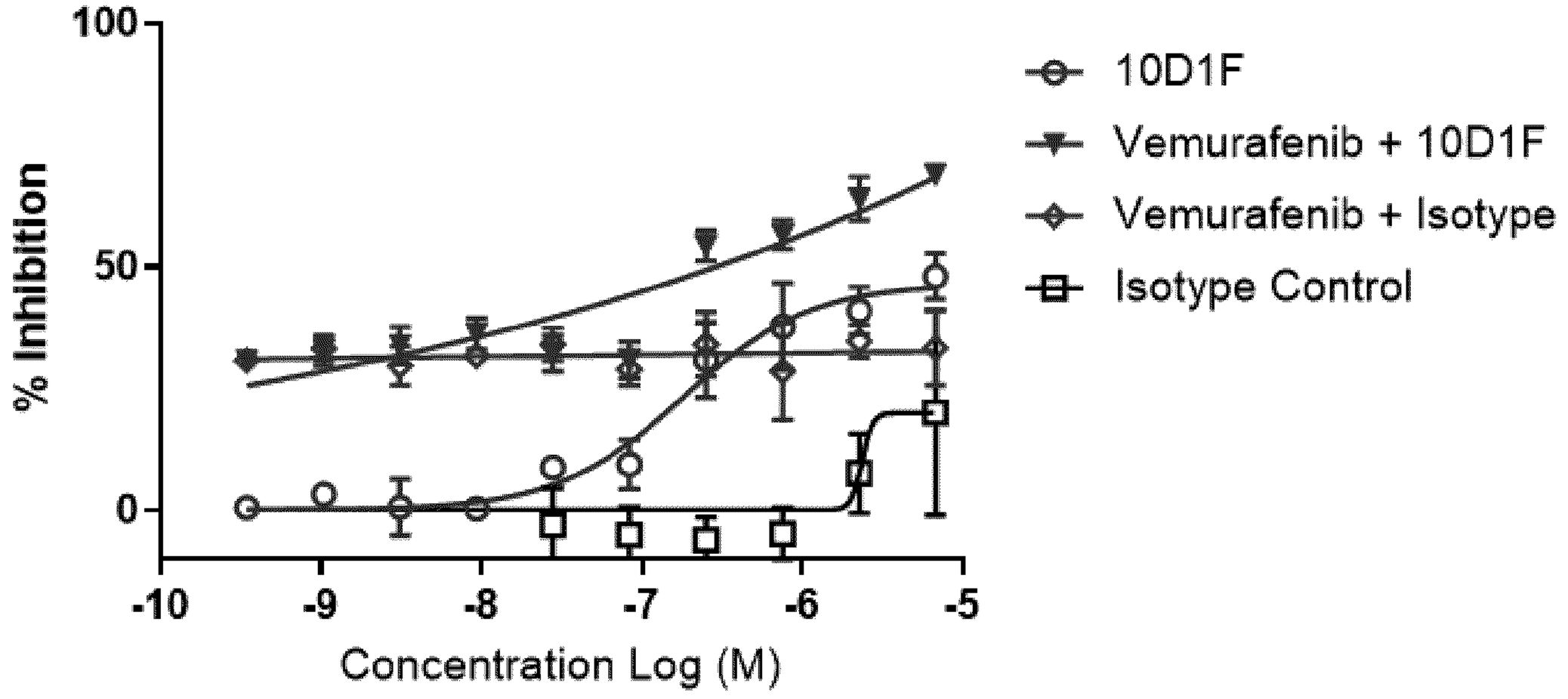


Figure 68B

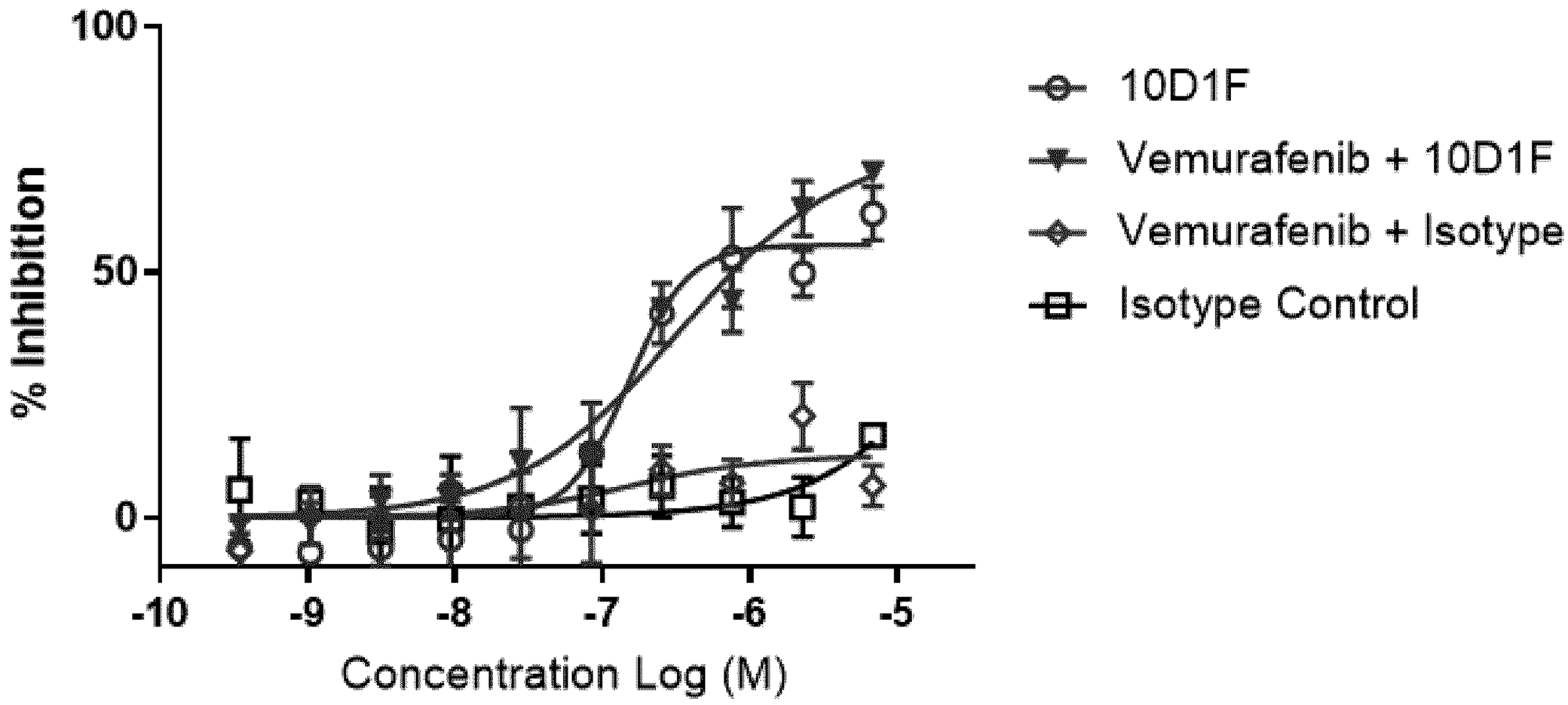


Figure 68C

Treatment Arm	Dose	Red Blood Cell						
		RBC Count (10^9/L)	Hemoglobin (g/dl)	Hematocrit (%)	Anemia Parameters			Platelet count (10^9/L)
					MCV (fml)	MCH (pg)	MCHC (g/dl)	
Vehicle	0	10.59	17.075	52.9275	50	16.125	32.25	490.5
10D1F	10 mg/kg	10.74	17.23	55.97	52.00	16.07	30.87	574.00
	25 mg/kg	10.55	16.97	53.37	50.33	16.10	31.87	555.00
	100 mg/kg	10.16	15.90	51.20	50.33	15.63	31.10	378.00
	250 mg/kg	10.32	16.97	52.13	50.33	16.43	32.53	501.67

Figure 69A

Treatment Arm	Dose	White Blood Cell			
		WBC Count (10^9/ L)	Lymphocyte Count (10^9/ L)	Monocyte Count (10^9/ L)	Neutrophil Count (10^9/ L)
Vehicle	0	7.43	5.58	0.30	1.55
10D1F	10 mg/kg	9.30	7.06	0.14	2.10
	25 mg/kg	8.00	5.94	0.31	1.74
	100 mg/kg	6.92	5.19	0.41	1.31
	250 mg/kg	3.92	2.88	0.29	0.75

Figure 69B

Treatment Arm	Dose (mg/kg)	Time (hrs)	Biochemistry				
			Liver (U/L)			Kidney (mg/dL)	
			ALB	ALT	ALP	CREA	BUN
Vehicle	0	96	3.25	25.00	104.50	0.25	13.00
10D1F	10	336	3.26	22.67	109.33	0.30	11.33
	25		3.20	48.67	121.00	0.23	12.33
	100		3.43	27.00	101.33	0.23	11.00
	250		3.30	53.00	101.33	0.27	16.33

Treatment Arm	Dose	Biochemistry					
		Pancreas		Electrolytes			
		GLU (mg/dL)	AMY (U/L)	NA (meq/L)	K (meq/L)	P (mg/dL)	CA (mg/dL)
Vehicle	0	128.75	959.75	144.75	7.35	6.83	10.35
10D1F	10 mg/kg	91.00	904.67	143.00	8.07	6.67	10.30
	25 mg/kg	109.67	938.00	144.33	7.30	6.50	10.77
	100 mg/kg	119.00	862.00	148.33	7.47	5.53	10.57
	250 mg/kg	139.00	1407.67	146.67	7.83	5.33	10.30

Figure 69C

Treatment Arm	Time (hrs)	Red Blood Cell						
		RBC Count (10^9/L)	Hemoglobin (g/dl)	Hematocrit (%)	Anemia Parameters			Platelet count (10^9/L)
					MCV (fml)	MCH (pg)	MCHC (g/dl)	
Vehicle	0	5.30	13.21	54.84	59.33	17.20	28.63	398.0
	6	4.55	8.97	51.38	60.67	16.77	29.90	362.0
	24	5.84	13.59	39.51	56.67	18.03	30.77	411.3
	96	7.76	10.87	52.41	60.67	17.60	30.23	488.7
	168	5.81	11.49	42.31	59.67	17.27	29.90	573.7
	336	7.51	16.41	49.23	60.67	16.83	29.03	685.0
10D1F	0	12.13	13.05	66.59	55.50	17.10	26.20	339.5
	6	11.96	12.95	66.88	57.00	17.35	25.90	392.0
	24	8.05	15.20	49.68	62.00	18.90	30.60	248.5
	96	8.07	15.65	49.34	61.00	19.40	31.80	337.5
	168	6.25	12.40	40.99	65.50	19.80	30.20	577.0
	336	7.35	13.60	47.13	64.00	18.25	28.40	440.0

Figure 70A

Treatment Arm	Time (hrs)	White Blood Cell			
		WBC Count (10^9/ L)	Lymphocyte Count (10^9/ L)	Monocyte Count (10^9/ L)	Neutrophil Count (10^9/ L)
Vehicle	0	13.22	10.12	1.43	3.08
	6	8.09	9.01	1.20	2.57
	24	9.82	9.08	0.89	2.08
	96	7.61	7.59	0.97	1.97
	168	11.02	9.23	1.24	2.05
	336	9.67	6.14	0.64	2.06
10D1F	0	10.61	2.87	0.27	2.47
	6	13.40	5.57	0.99	1.84
	24	10.70	7.55	0.84	2.32
	96	10.24	8.04	0.71	1.49
	168	4.68	3.45	0.18	1.05
	336	11.04	9.02	0.62	1.40

Figure 70B

Treatment Arm	Dose (mg/kg)	Time (hrs)	Biochemistry			
			Liver (U/L)		Kidney (mg/dL)	
			ALB	ALP	CREA	BUN
Vehicle	0	0	4.80	6.77	0.40	10.00
		6	5.03	6.37	0.37	12.00
		24	3.87	6.57	0.40	12.33
		96	3.93	6.63	0.40	12.00
		168	4.70	6.90	0.40	10.67
		336	4.97	6.53	0.33	13.33
10D1F	250	0	5.05	5.55	0.30	13.50
		6	4.40	5.95	0.35	12.50
		24	4.30	7.40	0.40	12.50
		96	4.70	7.00	0.40	12.00
		168	5.00	6.50	0.55	13.50
		336	4.45	6.15	0.30	7.00

Treatment Arm	Time (hrs)	Biochemistry					
		Pancreas		Electrolytes			
		GLU (mg/dL)	AMY (U/L)	NA (meq/L)	K (meq/L)	P (mg/dL)	CA (mg/dL)
Vehicle	0	119.3	514.3	138.3	6.87	6.87	11.50
	6	141.0	537.3	142.7	5.73	5.00	11.50
	24	130.3	594.3	139.7	5.37	7.43	11.53
	96	117.0	503.3	141.3	5.90	7.17	11.60
	168	122.7	562.7	144.0	7.10	6.93	11.30
	336	135.7	643.0	139.7	6.27	7.80	11.17
10D1F	0	125.0	465.5	141.0	6.30	6.70	10.75
	6	123.5	521.0	143.5	6.00	7.25	11.05
	24	131.0	646.5	140.5	7.05	7.85	11.75
	96	111.0	632.5	140.0	6.85	8.05	11.85
	168	146.0	574.0	137.0	5.30	7.05	11.20
	336	100.5	821.5	139.0	5.35	7.30	11.45

Figure 70C

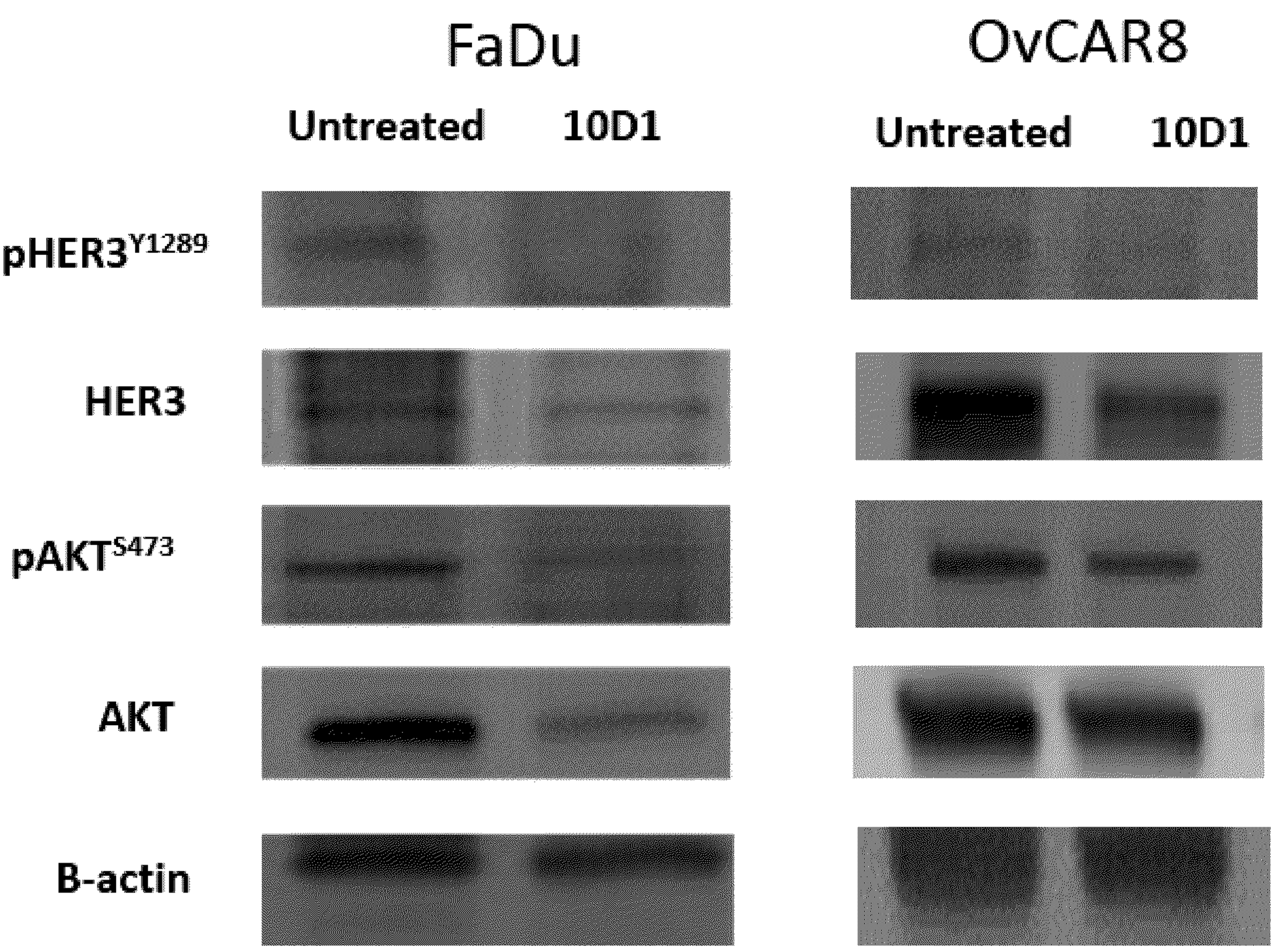

FaDu
Untreated
10D1
OvCAR8
Untreated
10D1
pHER3Y1289
HER3
pAKTS473
AKT
B-actin

Figure 71

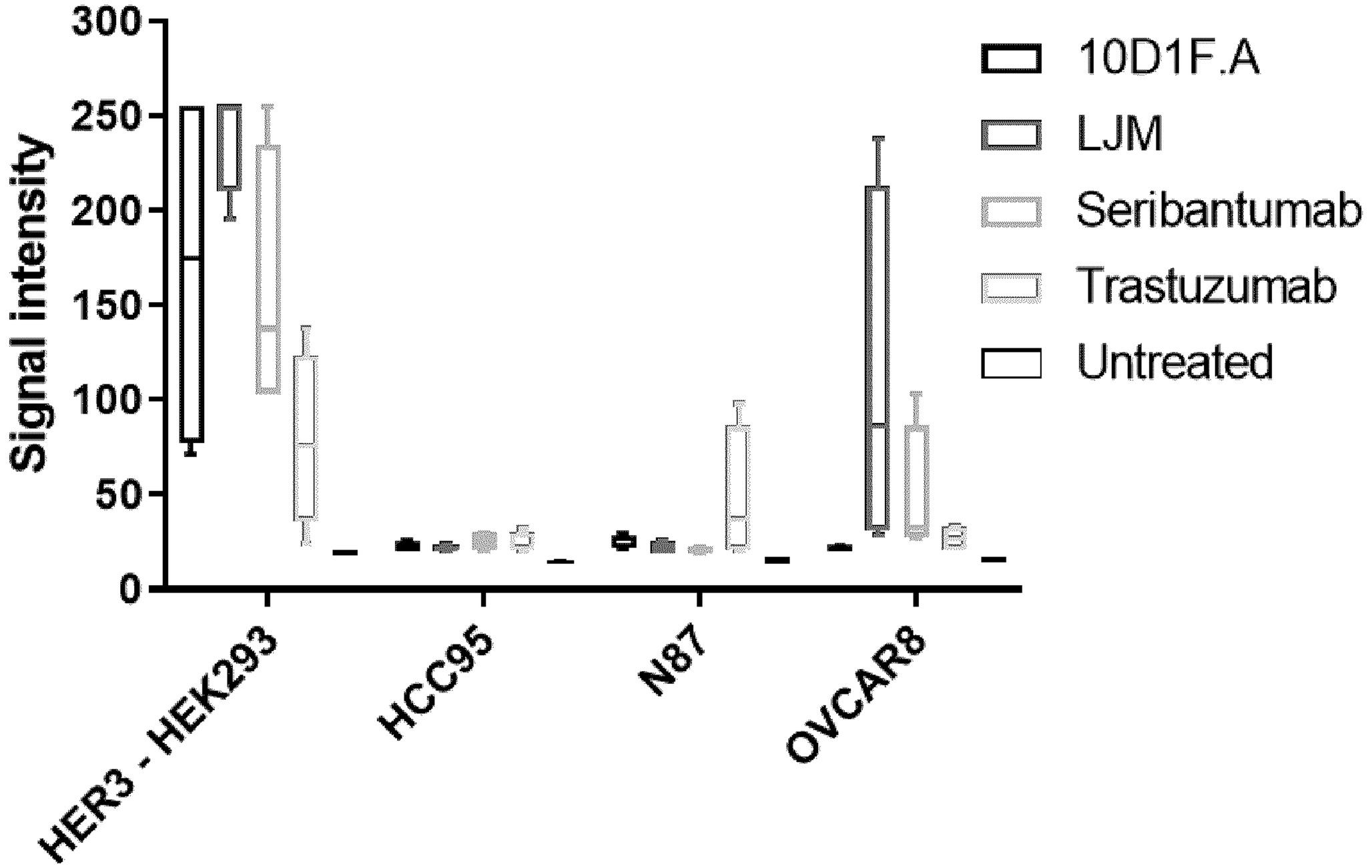

Maximum FITC signal (24h)
Signal intensity
300
250
200
150
100
50
0
HER3 - HEK293
HCC95
N87
OVCAR8
10D1F.A
LJM
Seribantumab
Trastuzumab
Untreated

Figure 72

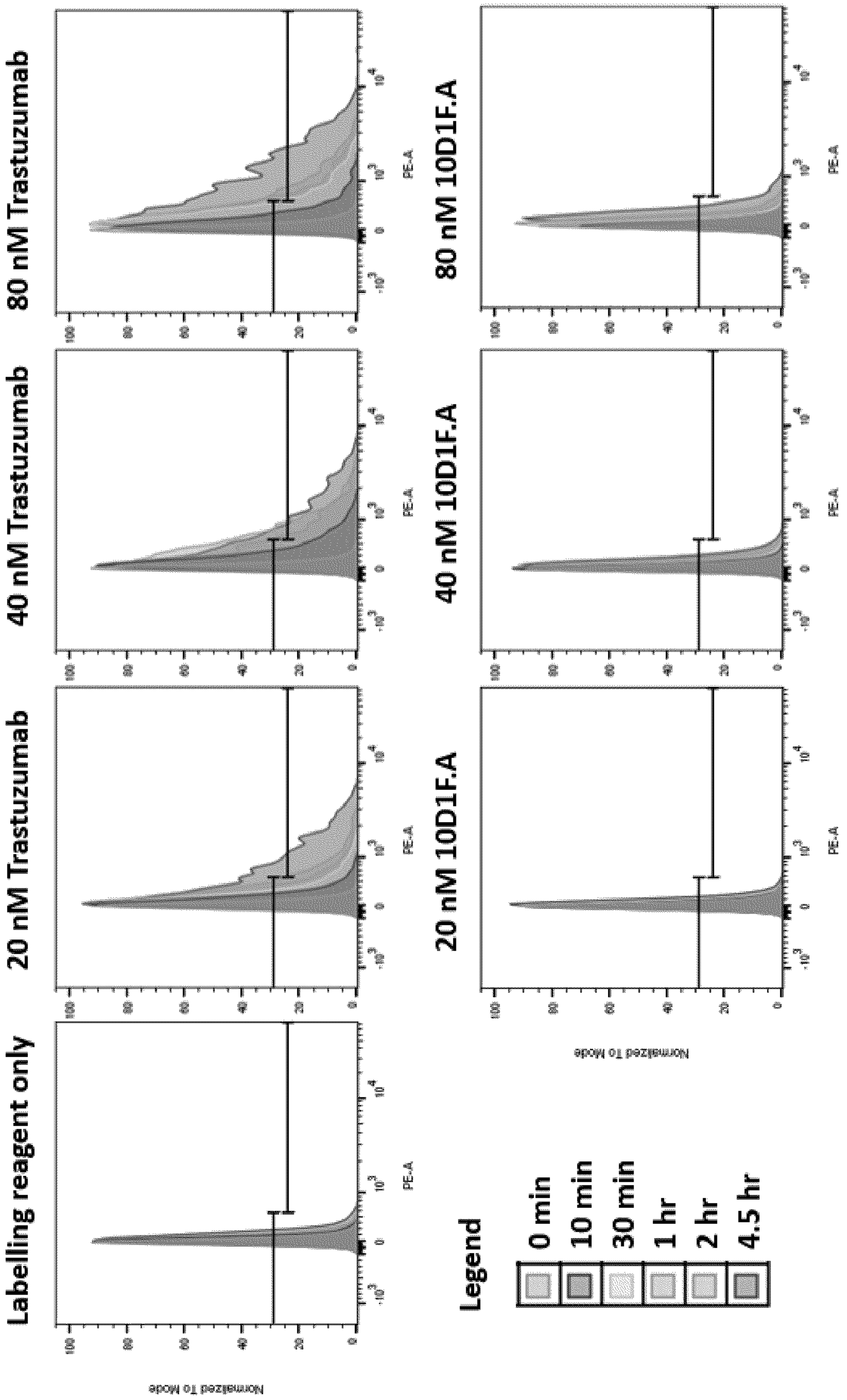

Labelling reagent only
20 nM Trastuzumab
20 nM 10D1F.A
40 nM Trastuzumab
40 nM 10D1F.A
80 nM Trastuzumab
80 nM 10D1F.A
Normalized To Mode
PE-A
Legend
0 min
10 min
30 min
1 hr
2 hr
4.5 hr

Figure 73

MFI

	0 min	10 min	30 min	1 hr	2 hrs	4.5 hrs
80 nM 10D1F.A	110	108	129	148	184	279
40 nM 10D1F.A	104	114	129	145	178	204
20 nM 10D1F.A	105	110	117	119	127	156
80 nM Trastuzumab	133	270	393	435	528	802
40 nM Trastuzumab	124	298	294	495	465	614
20 nM Trastuzumab	115	194	266	305	354	578
No Ab + 120 nM Zenon	102	116	117	128	143	182

Percent of PE+ cells

	0 min	10 min	30 min	1 hr	2 hrs	4.5 hrs
80 nM 10D1F.A	0.13 %	0 %	0.26 %	0.50 %	0.97 %	6.43 %
40 nM 10D1F.A	0.14 %	0.21 %	0.37 %	0.38 %	1.01 %	1.72 %
20 nM 10D1F.A	0.093 %	0.094 %	0 %	0.18 %	0.22 %	0.43 %
80 nM Trastuzumab	0.90 %	9.64 %	21.7 %	26.9 %	35.6 %	56.0 %
40 nM Trastuzumab	0.49 %	14.4 %	13.2 %	34.3 %	31.4 %	42.5 %
20 nM Trastuzumab	0.14 %	3.73 %	11.1 %	15.2 %	20.3 %	41.8 %
No Ab + 120 nM Zenon	0.039 %	0.086 %	0.35 %	0.18 %	0.26 %	1.06 %

Figure 73B

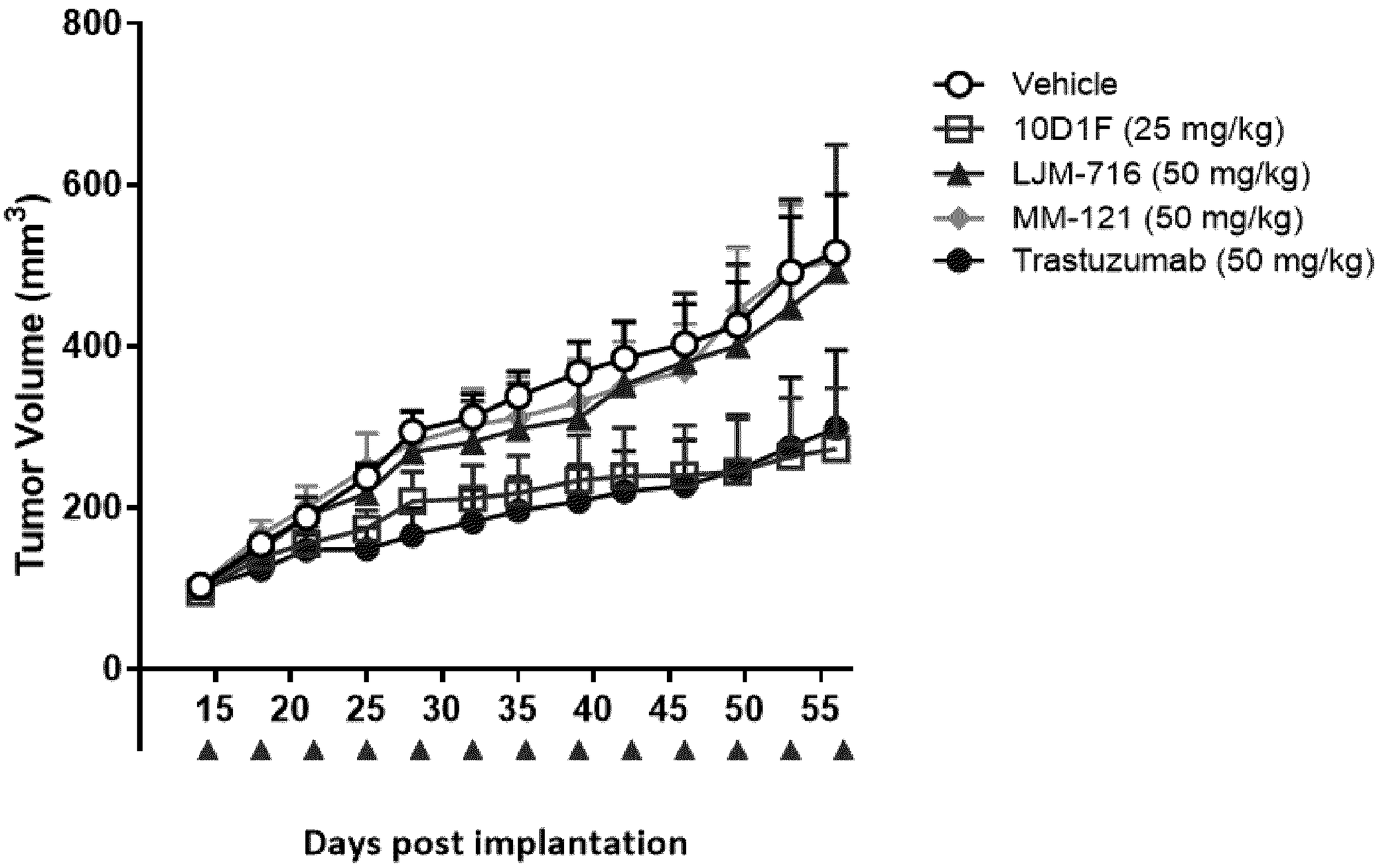

Vehicle
10D1F (25 mg/kg)
LJM-716 (50 mg/kg)
MM-121 (50 mg/kg)
Trastuzumab (50 mg/kg)
Tumor Volume (mm3)
800
600
400
200
0
15
20
25
30
35
40
45
50
55
Days post implantation

Figure 74

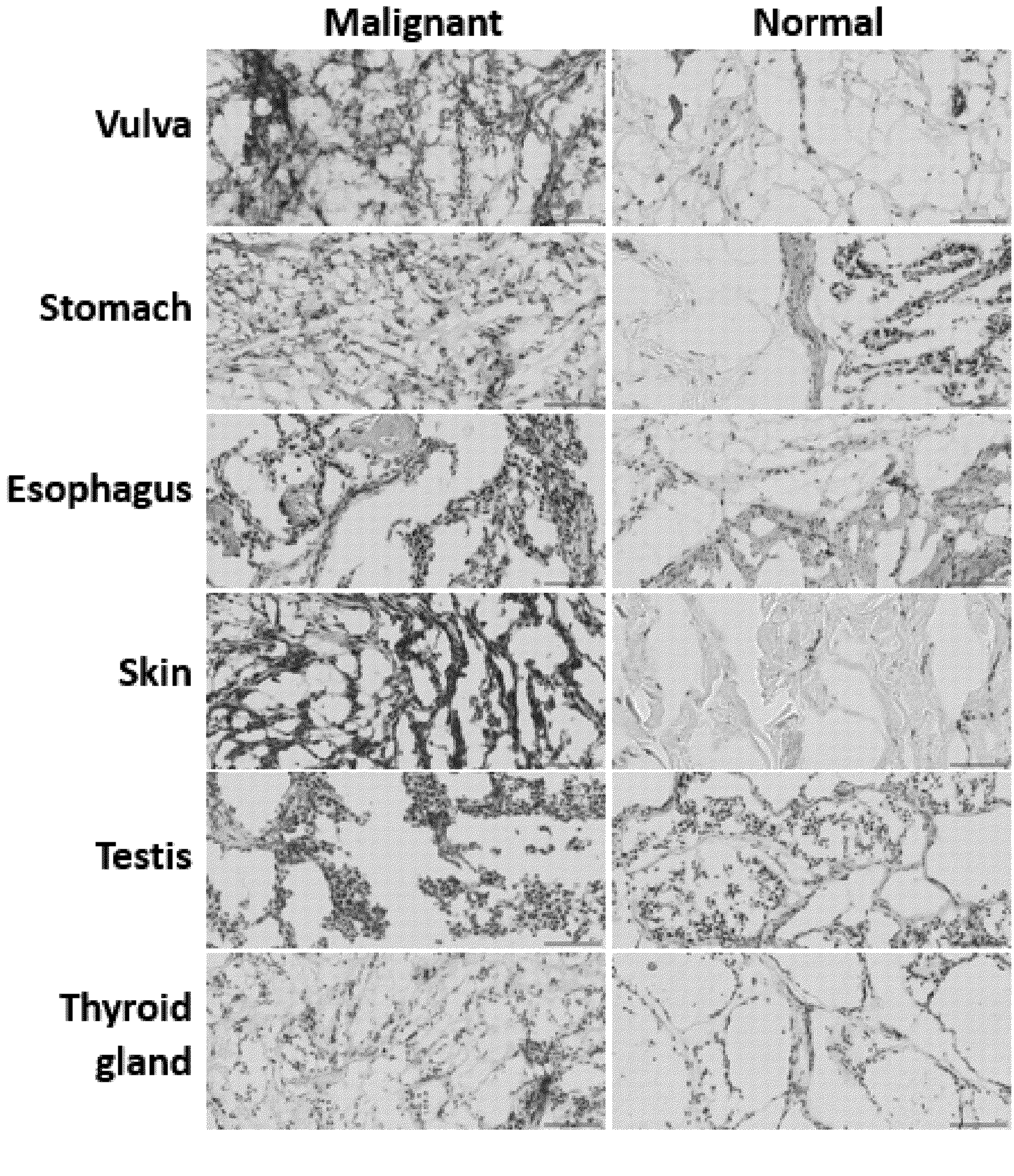

Malignant
Normal
Vulva
Stomach
Esophagus
Skin
Testis
Thyroid gland

Figure 75A

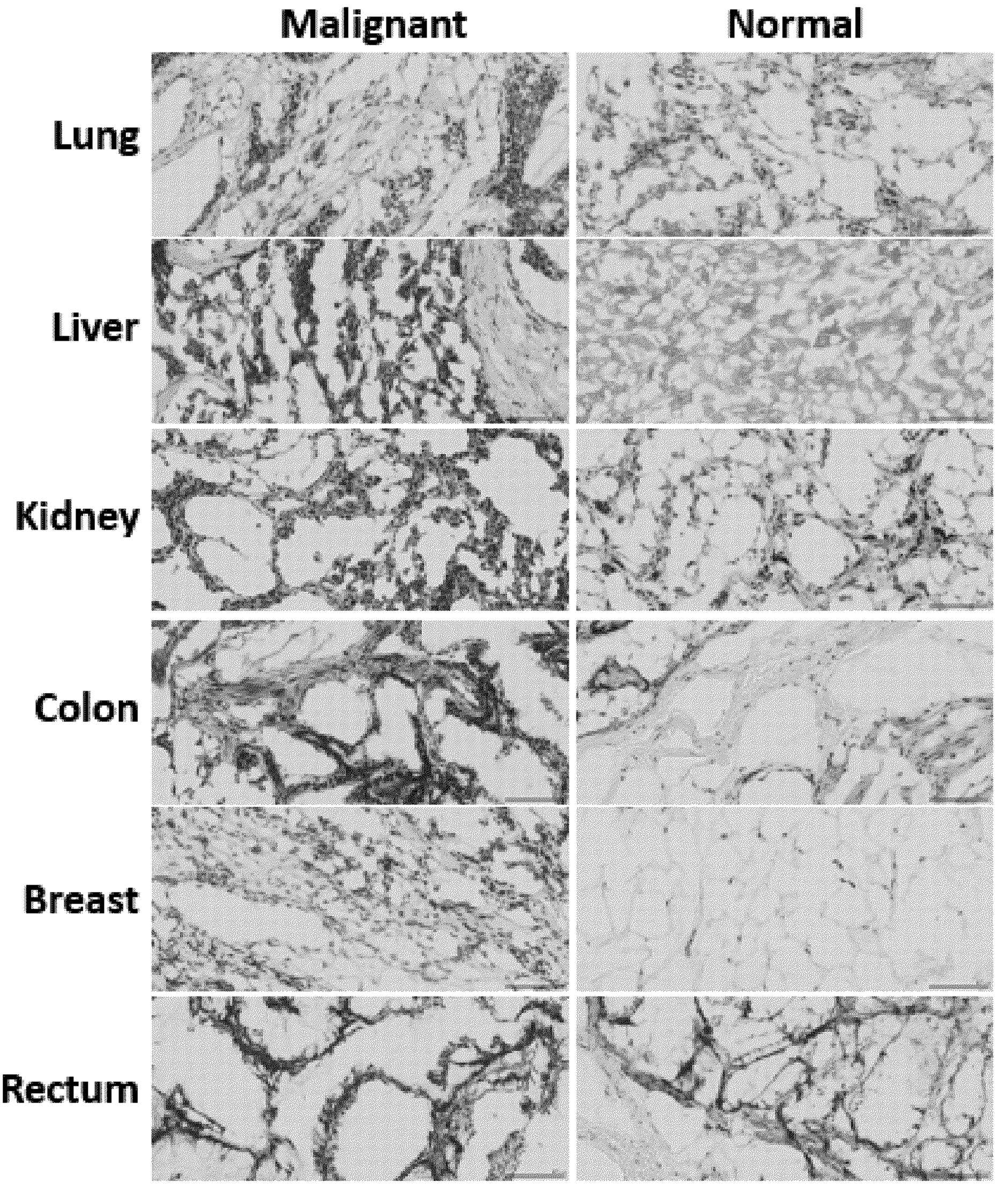


Figure 75B

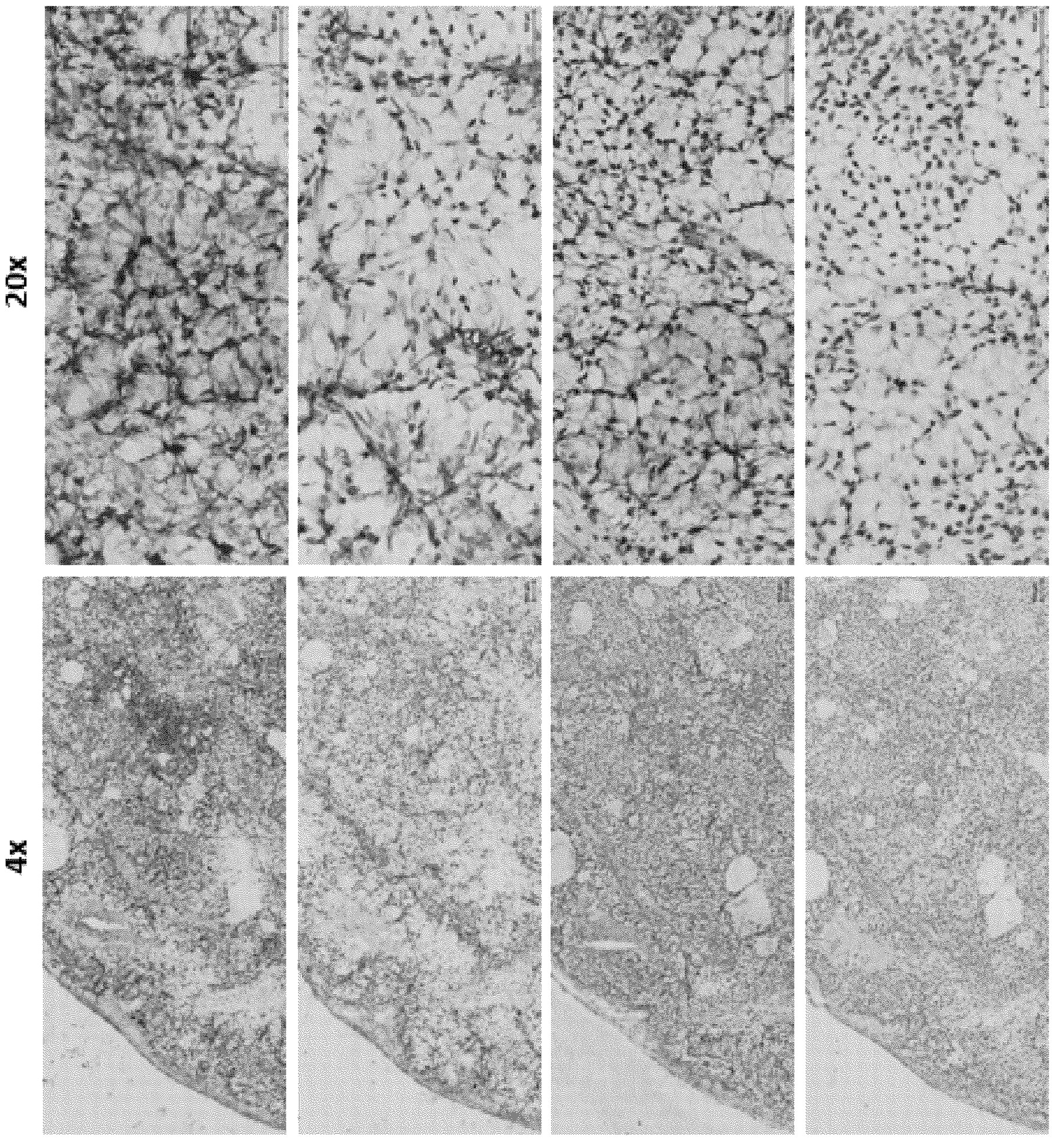

20x
4x
Rabbit anti-HER3 (Sino)
+
Goat anti-rabbit HRP
No primary
+
Goat anti-rabbit HRP
10D1F
+
Goat anti-human HRP
No primary
+
Goat anti-human HRP

Figure 76

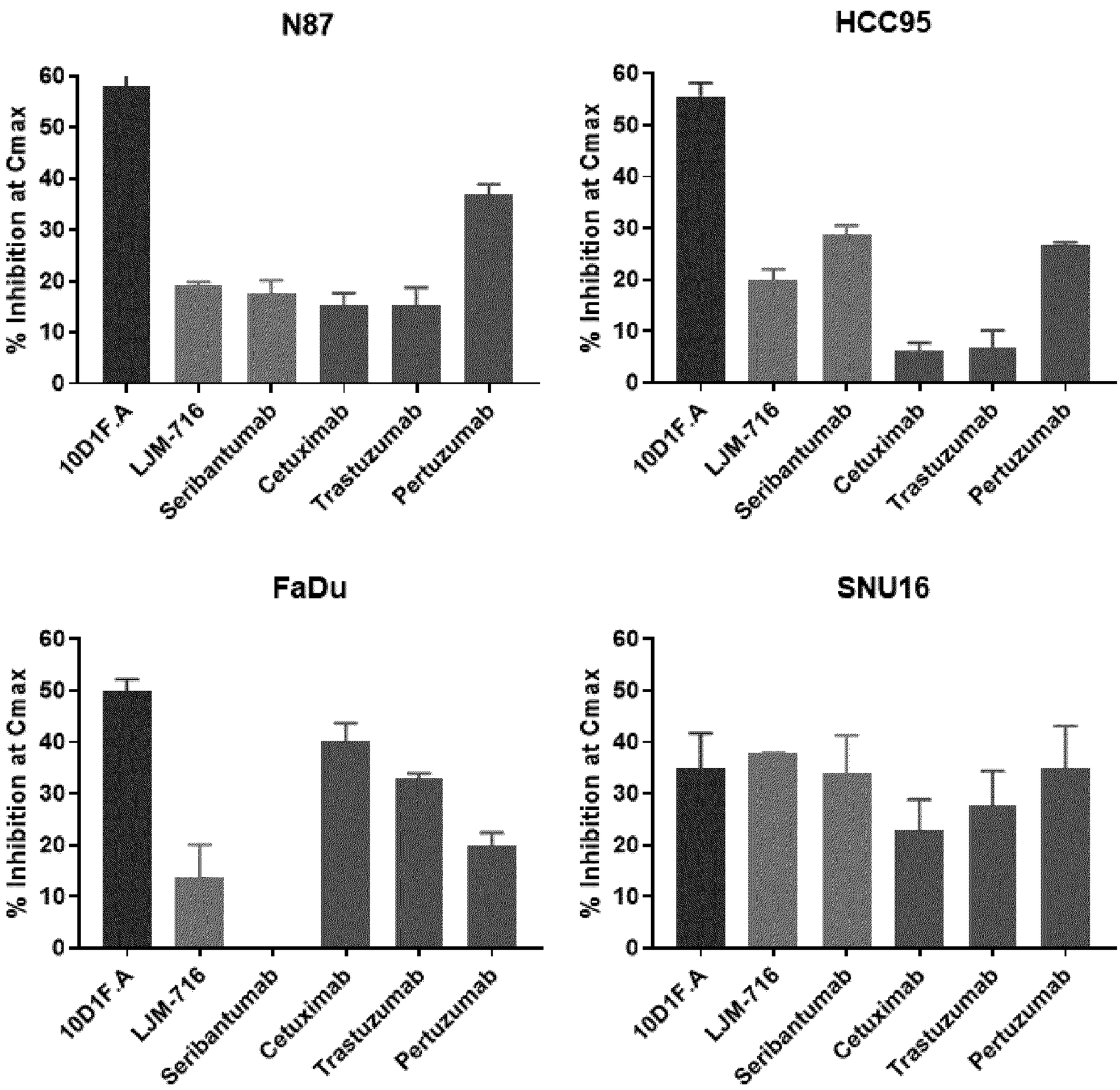

N87
HCC95
% Inhibition at Cmax
0
10
20
30
40
50
60
10D1F.A
LJM-716
Seribantumab
Cetuximab
Trastuzumab
Pertuzumab
FaDu
SNU16

Figure 77A

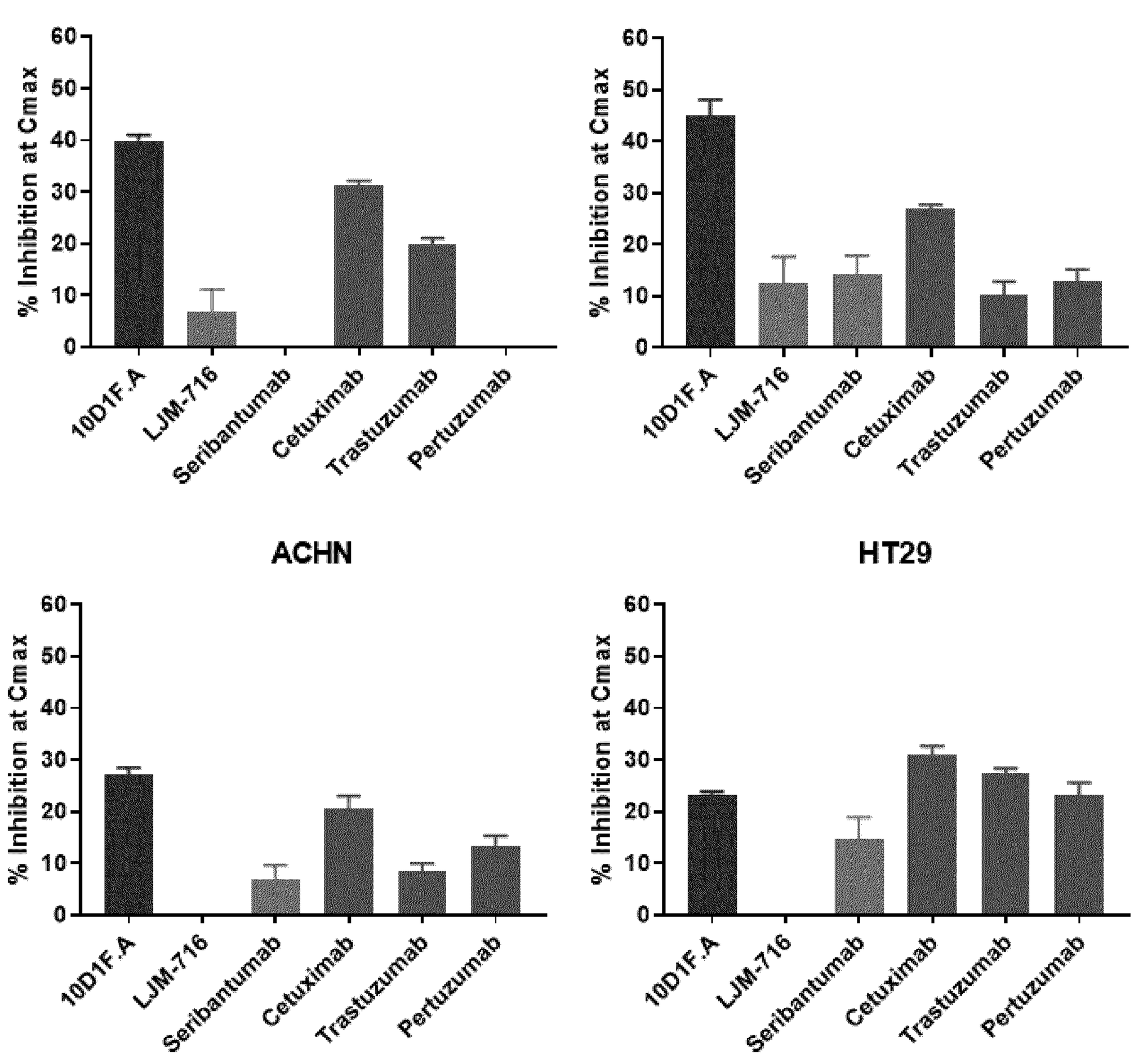
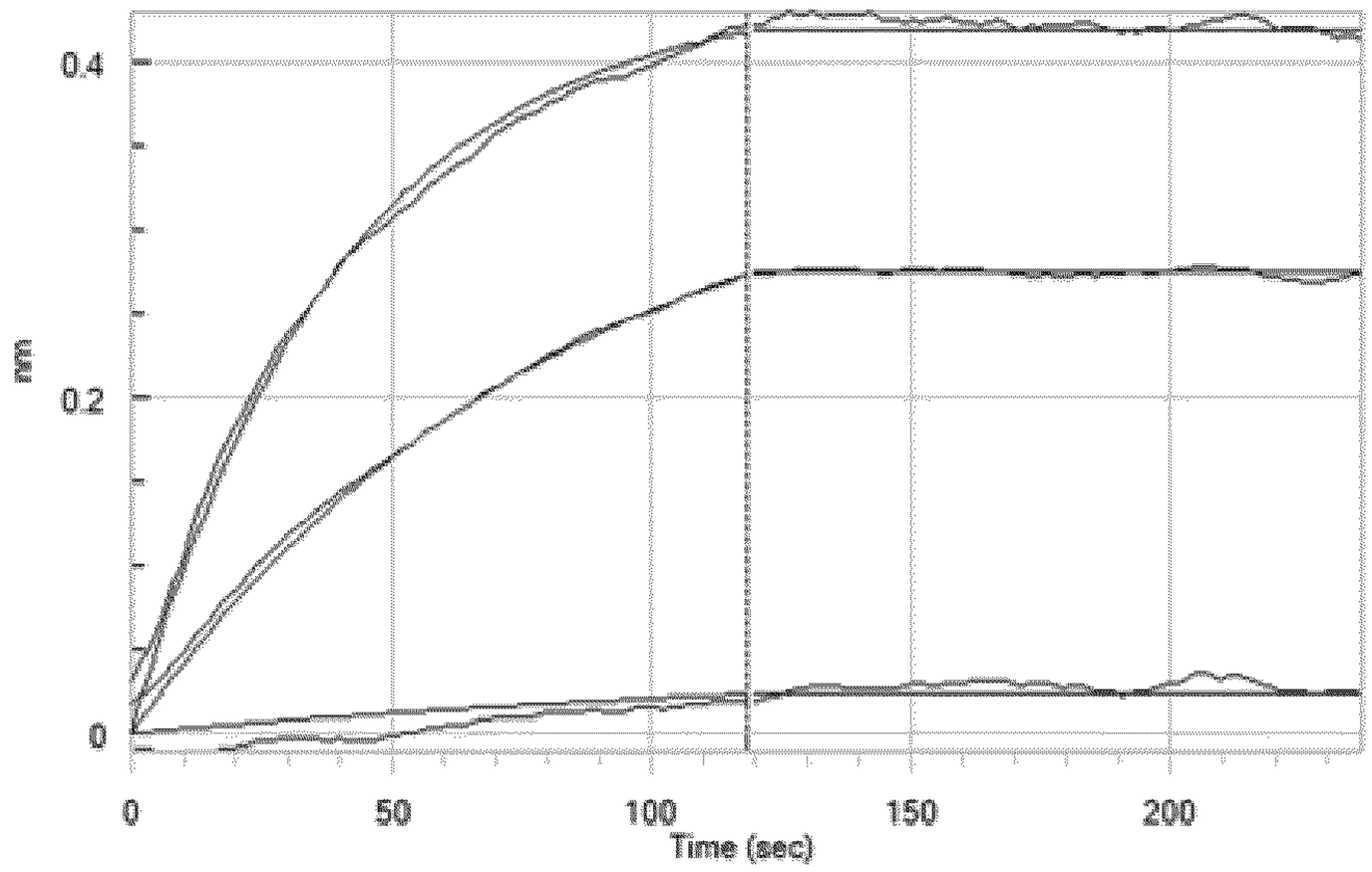
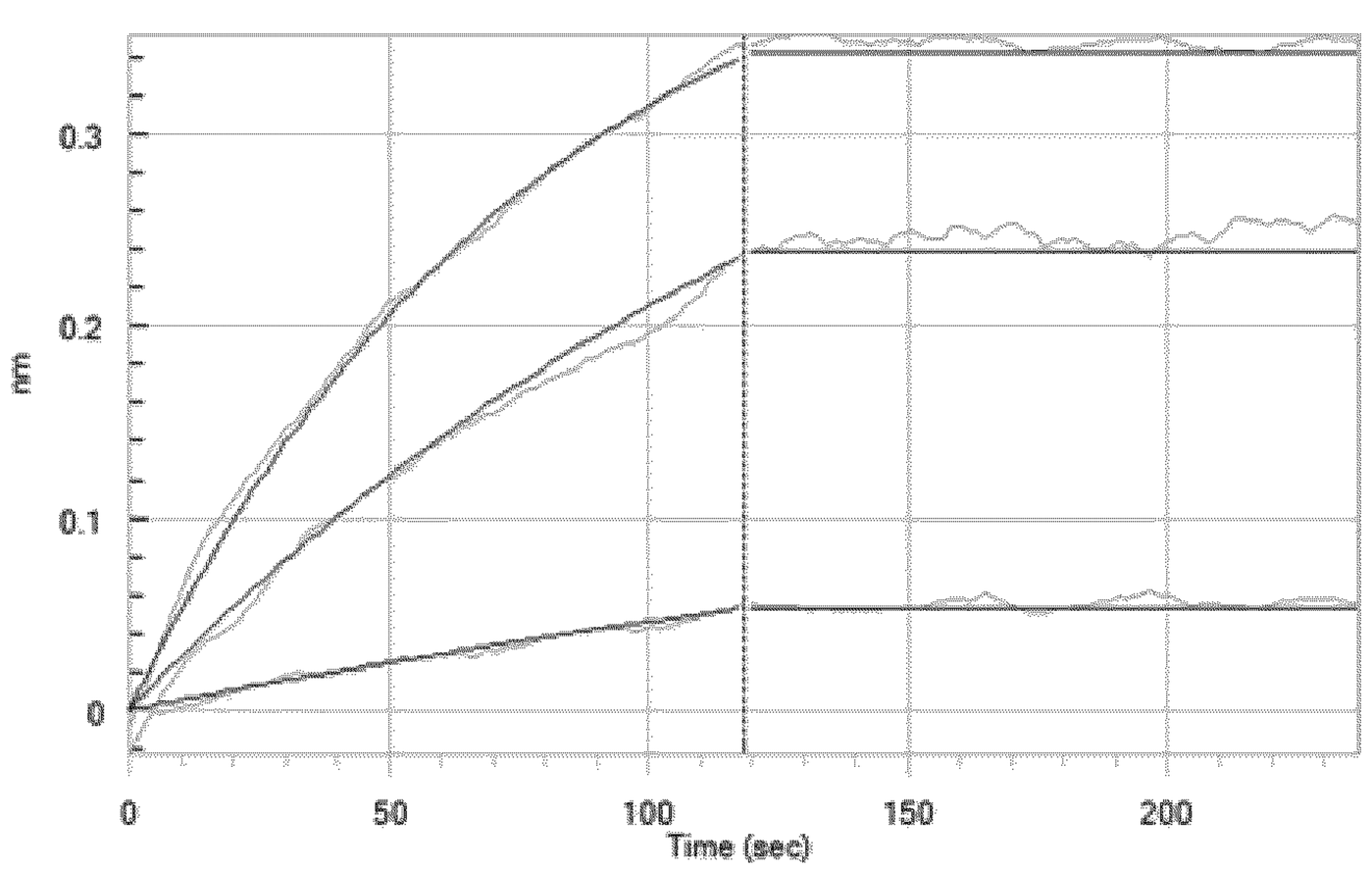

A549
OvCar8
ACHN
HT29
% Inhibition at Cmax
0
10
20
30
40
50
60
10D1F.A
LJM-716
Seribantumab
Cetuximab
Trastuzumab
Pertuzumab

Figure 77B



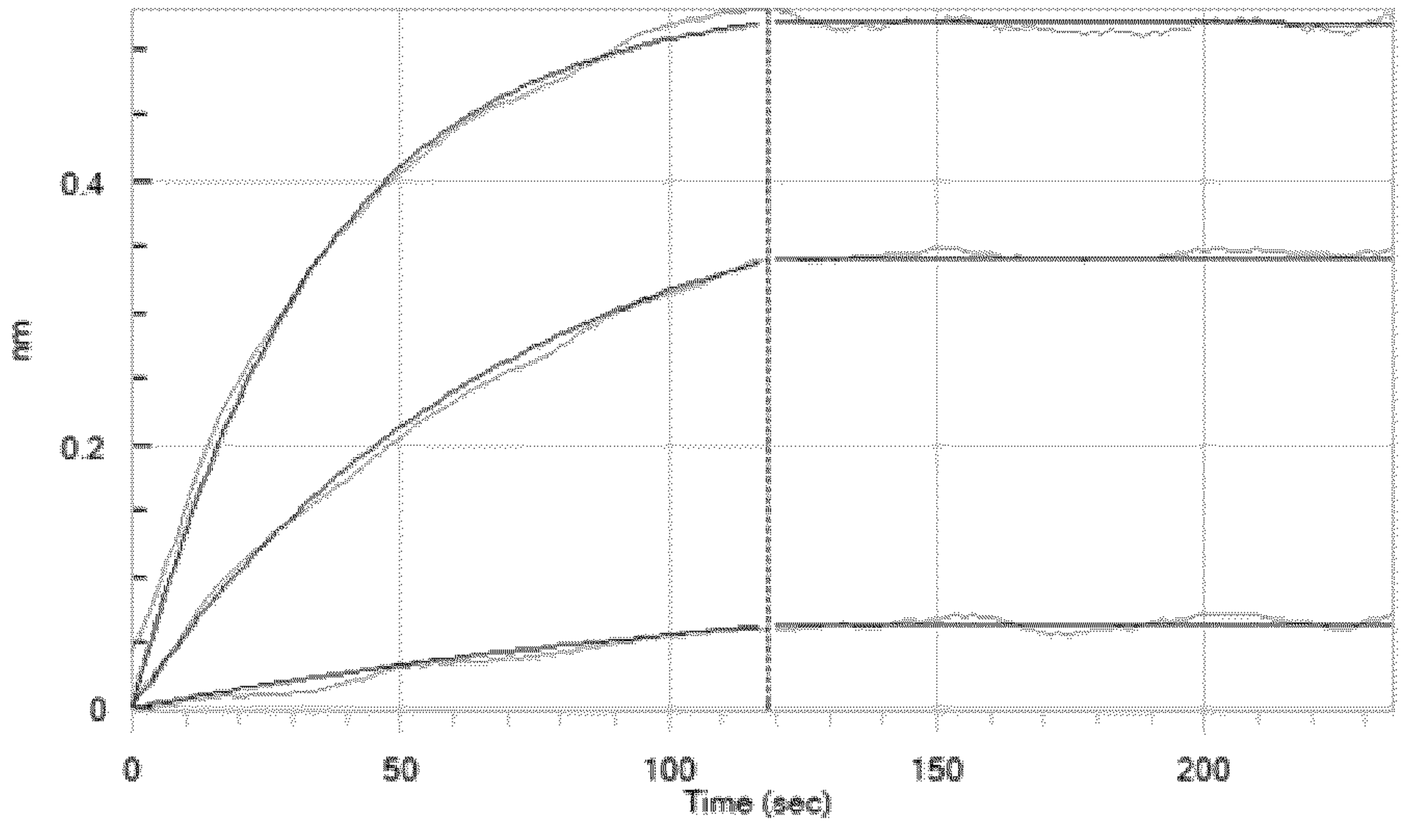
k_{on} (M^{-1} s^{-1})	K_d	k_{dis} (s^{-1})
1.99 E5	**< 1 pM**	< 1E-7

Figure 78A



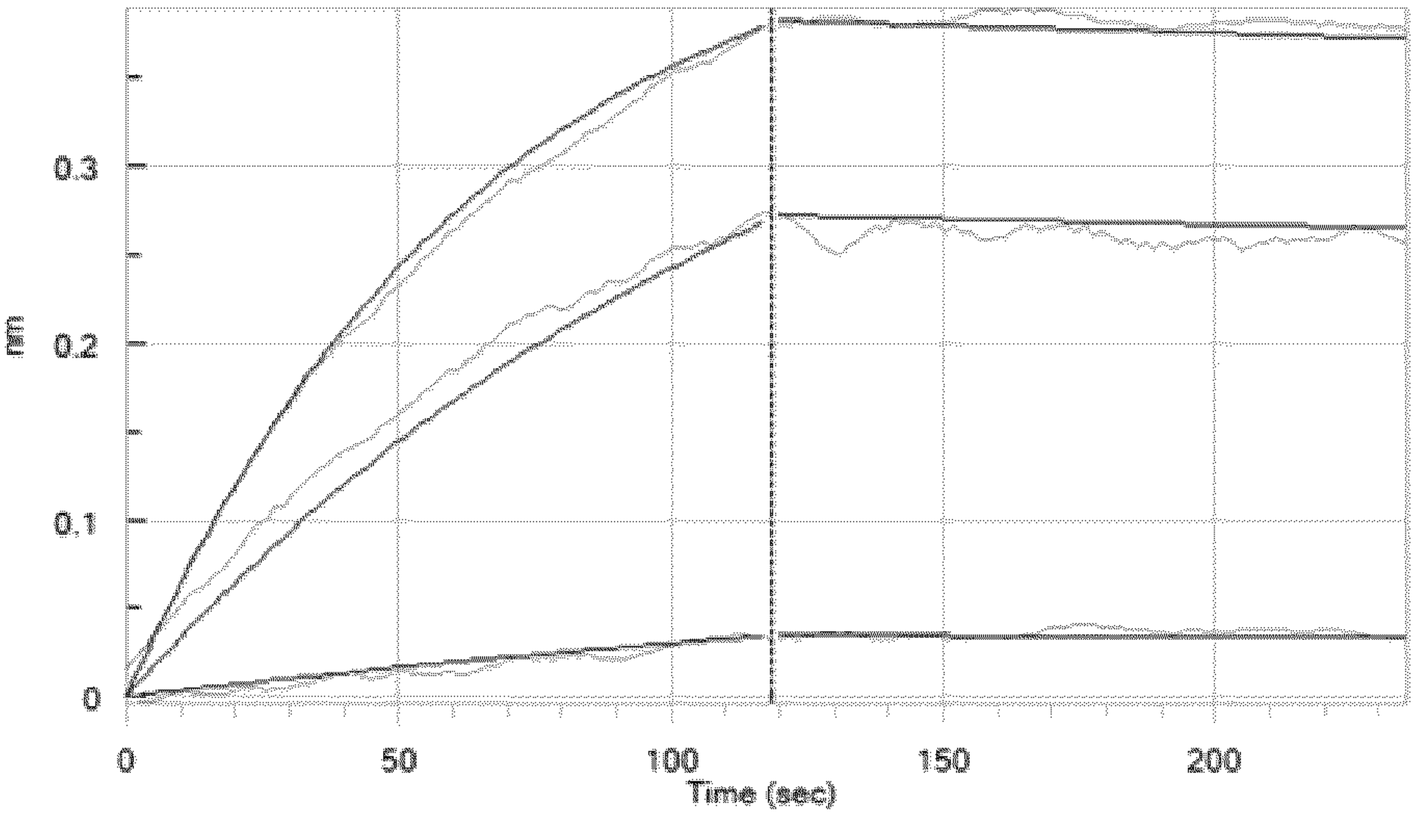
k_{on} (M^{-1} s^{-1})	K_d	k_{dis} (s^{-1})
1.99 E5	**< 1 pM**	< 1E-7

Figure 78B



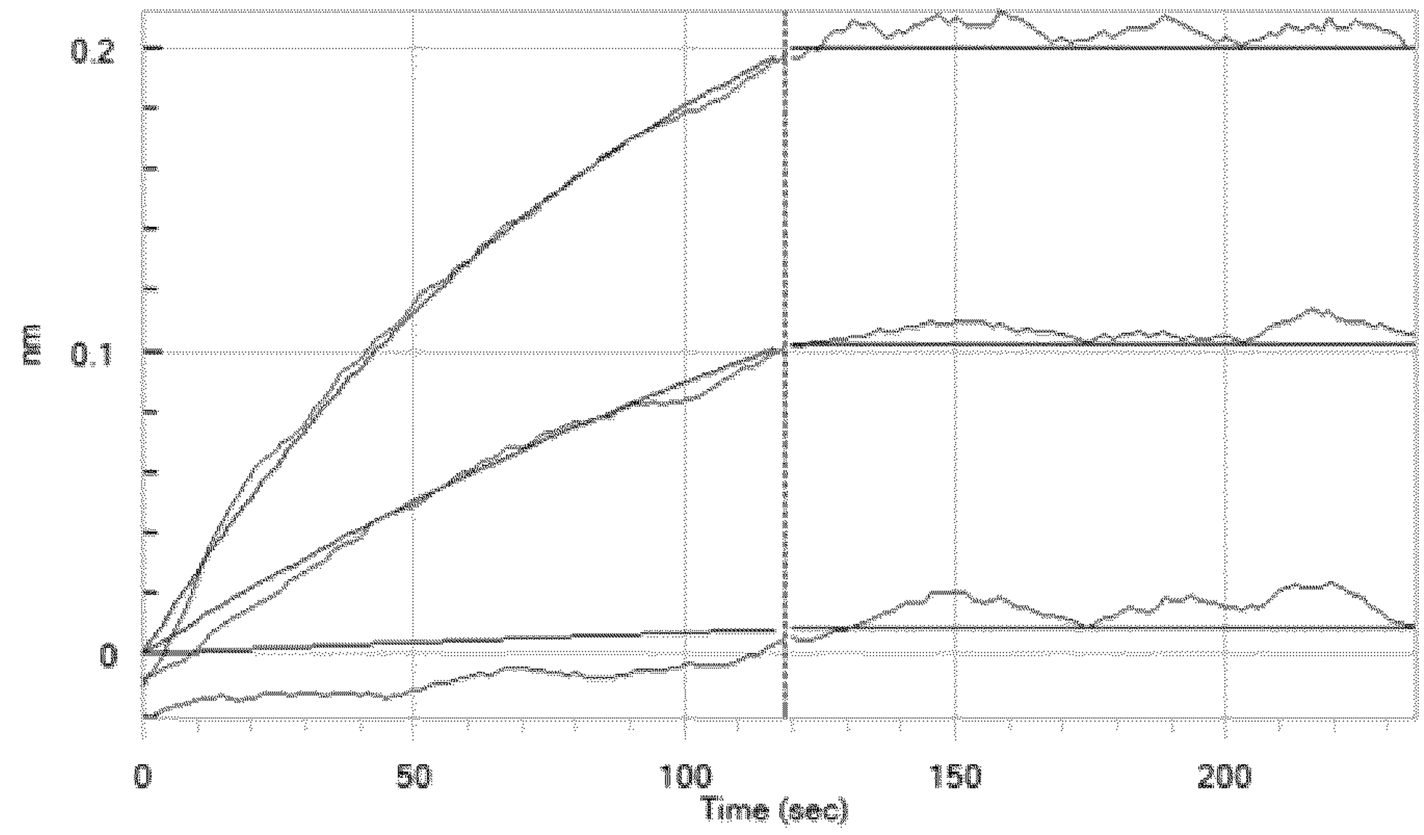
k_{on} (M^{-1} s^{-1})	K_d	k_{dis} (s^{-1})
2.3 E5	**0.73 nM**	1.68 E-5

Figure 78C



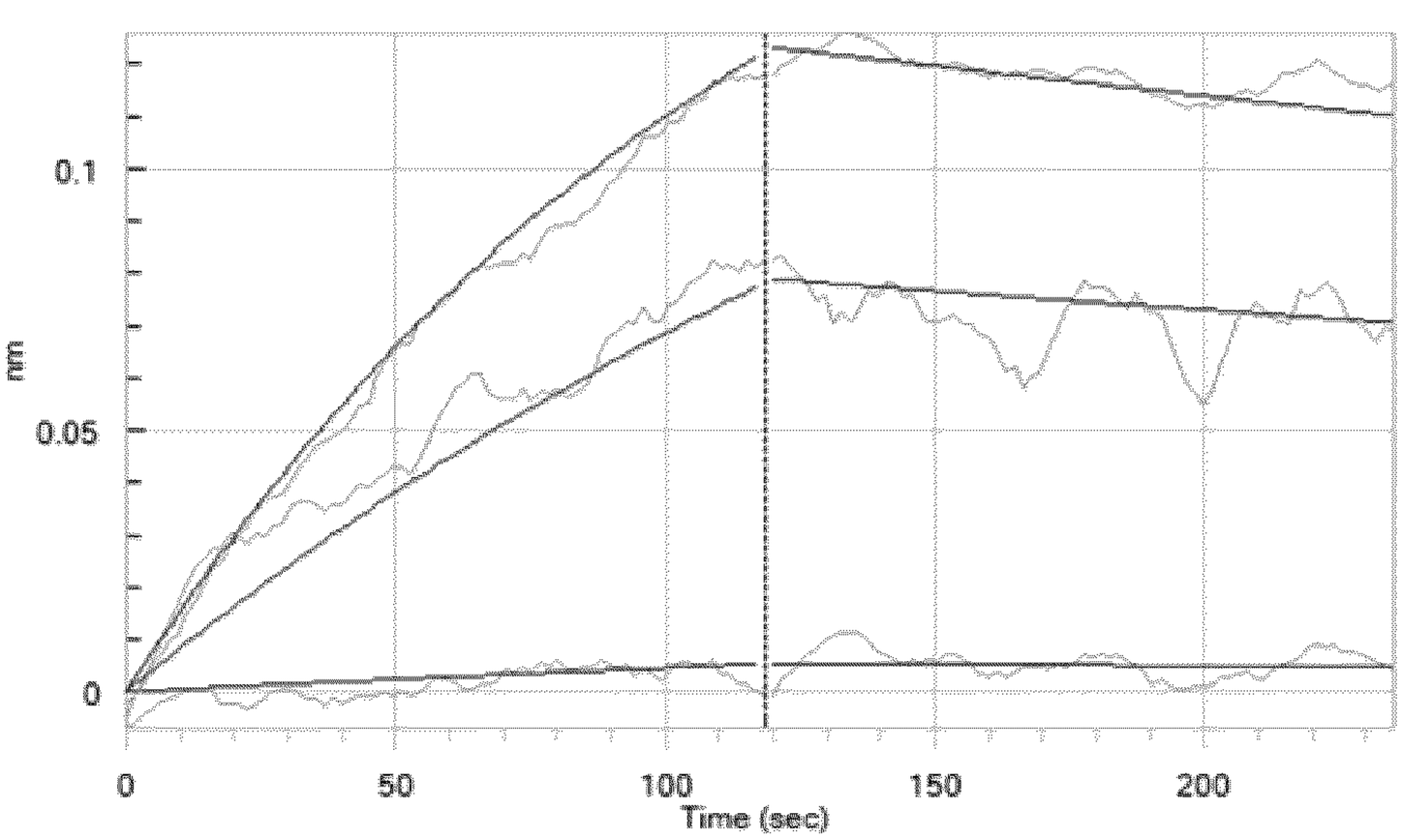
k_{on} (M^{-1} s^{-1})	K_d	k_{dis} (s^{-1})
1.2 E5	**1.92 nM**	2.31 E-4

Figure 78D



k_{on} (M^{-1} s^{-1})	K_d	k_{dis} (s^{-1})
7.98 E4	**< 1 pM**	< 1E-7

Figure 78E



k_{on} (M^{-1} s^{-1})	K_d	k_{dis} (s^{-1})
5.75 E4	**16.8 nM**	9.66E-4

Figure 78F

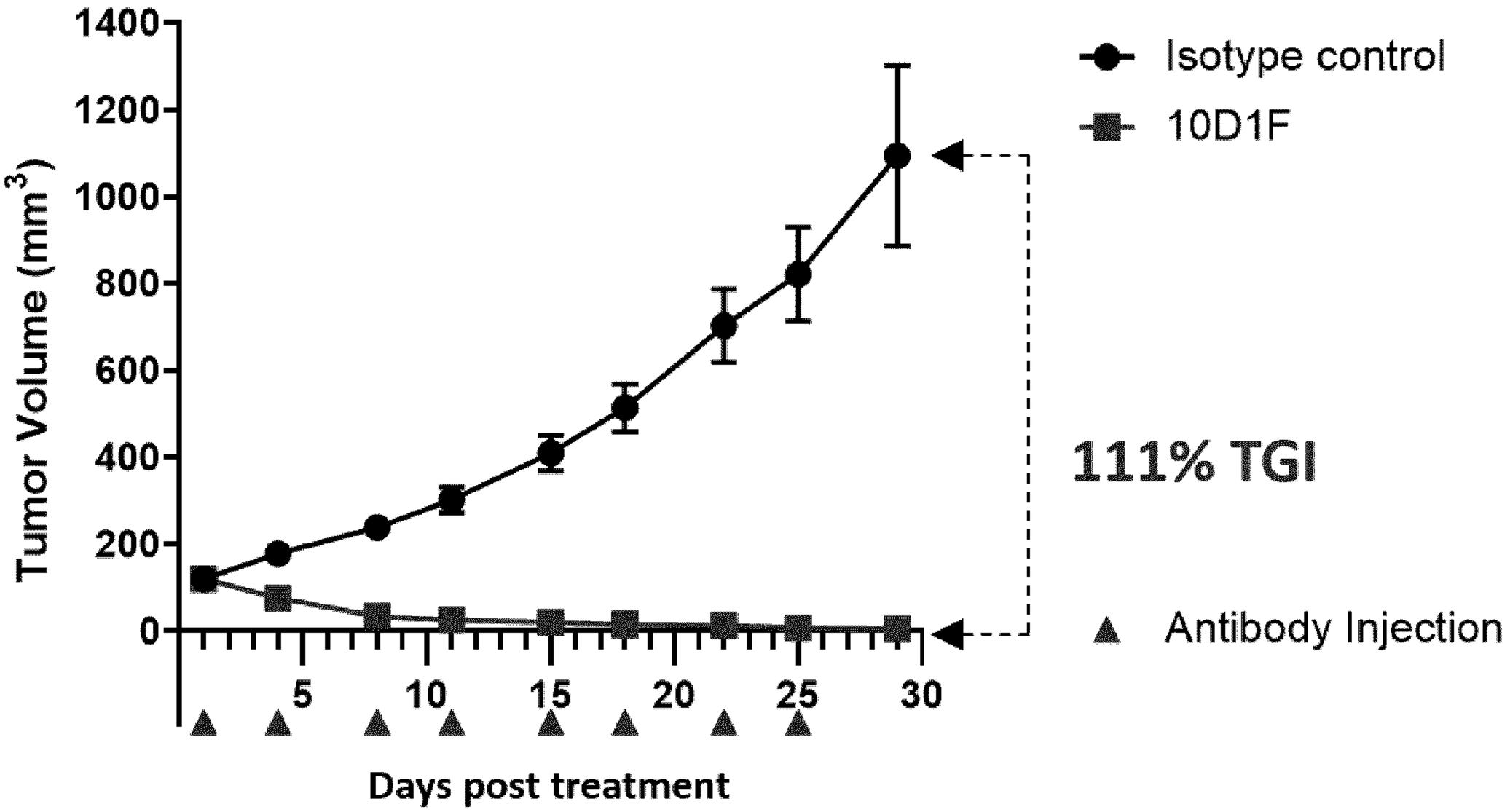

1400
1200
1000
800
600
400
200
0
Tumor Volume (mm3)
5
10
15
20
25
30
Days post treatment
Isotype control
10D1F
111% TGI
Antibody Injection

Figure 79