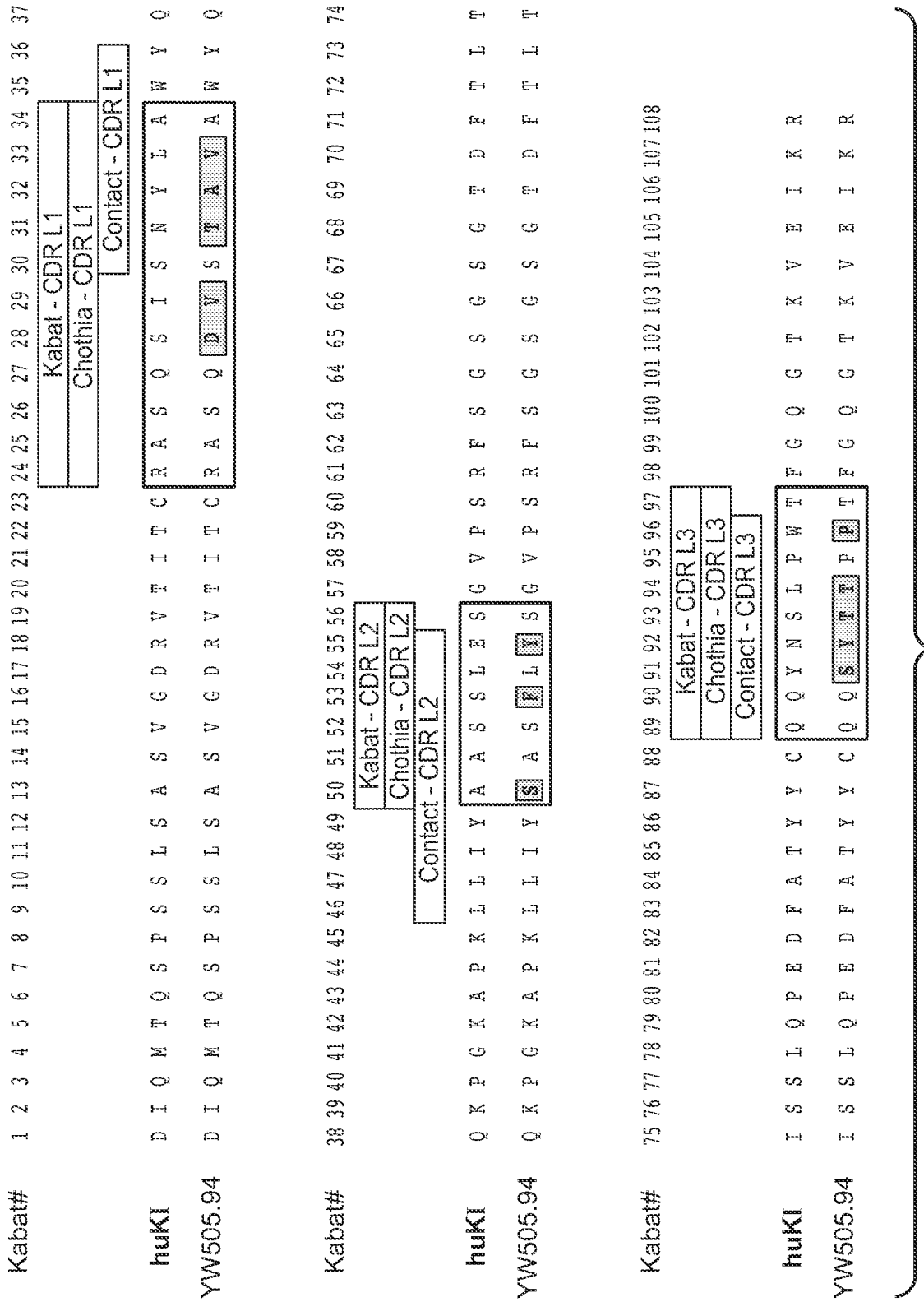

Kabat - CDR L1
Chothia - CDR L1
Contact - CDR L1
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
Kabat#
huKI
YW505.94

FIG. 1A

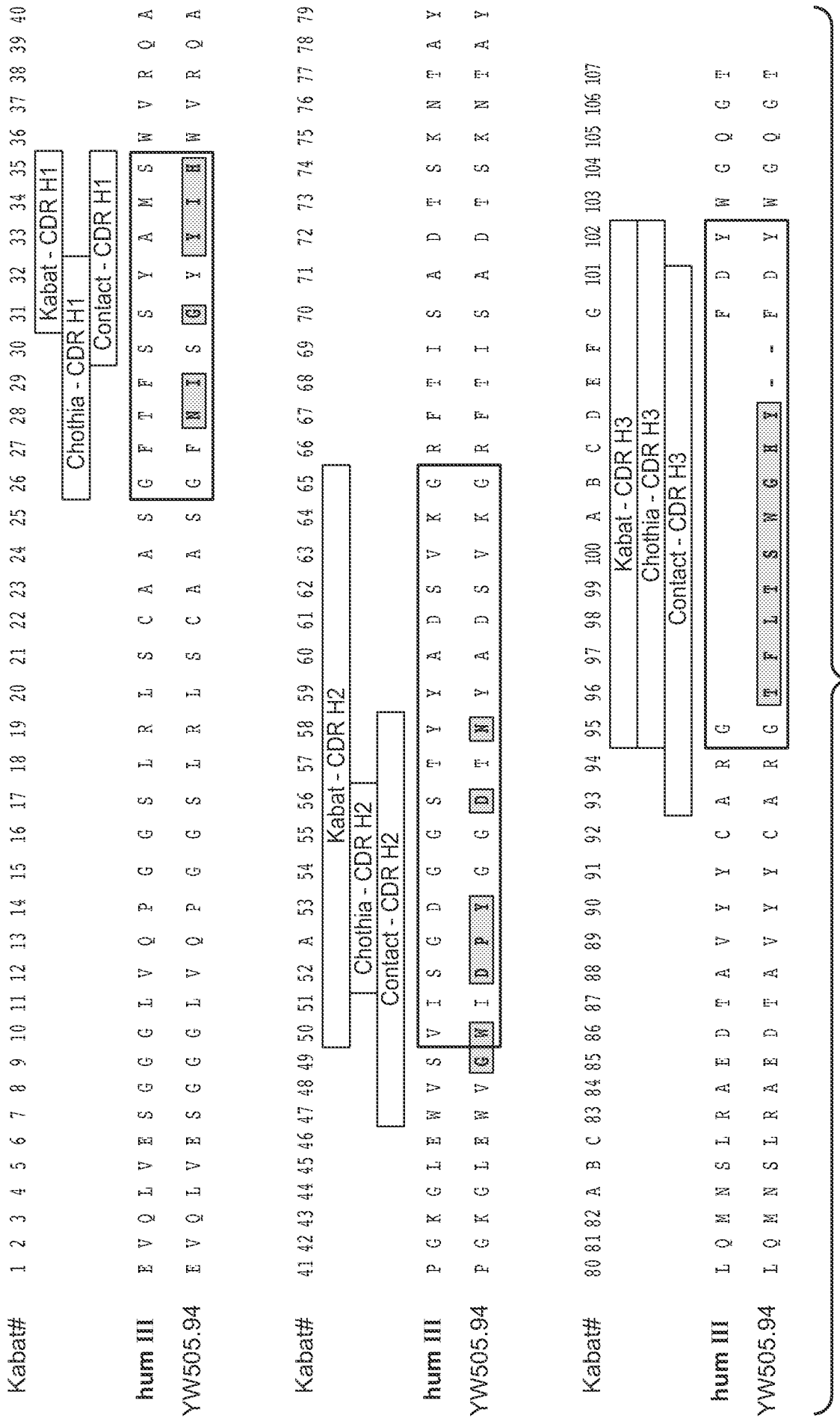

Kabat#
hum III
YW505.94
Kabat - CDR H1
Chothia - CDR H1
Contact - CDR H1
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3

FIG. 1B

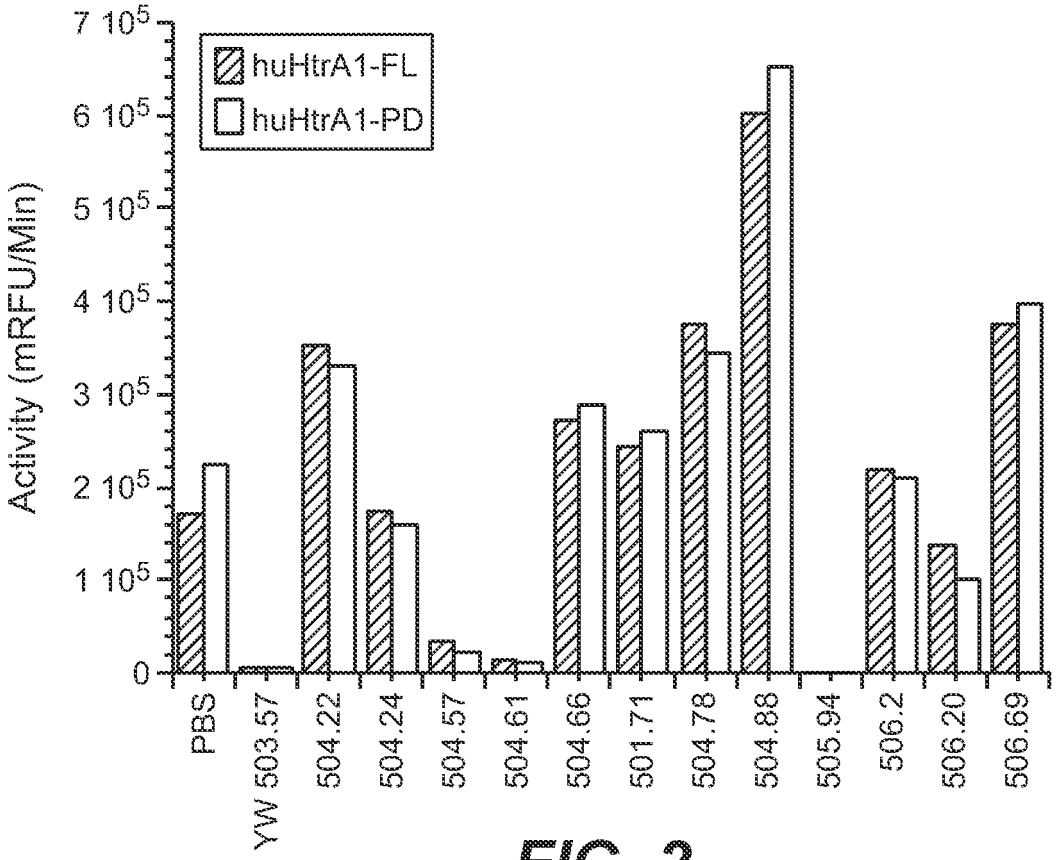

7 10^5
6 10^5
5 10^5
4 10^5
3 10^5
2 10^5
1 10^5
0
Activity (mRFU/Min)
huHtrA1-FL
huHtrA1-PD
PBS
YW 503.57
504.22
504.24
504.57
504.61
504.66
501.71
504.78
504.88
505.94
506.2
506.20
506.69

FIG. 2

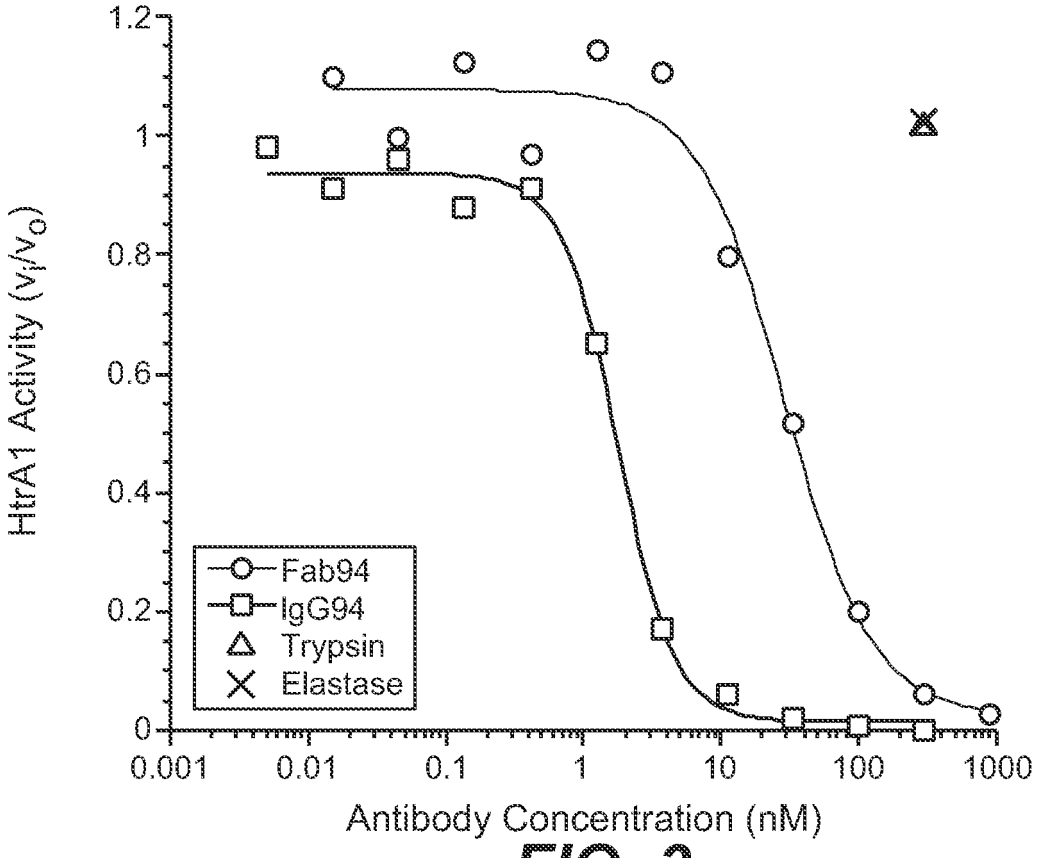

1.2
1
0.8
0.6
0.4
0.2
0
HtrA1 Activity (v_i/v_o)
Fab94
IgG94
Trypsin
Elastase
0.001
0.01
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 3

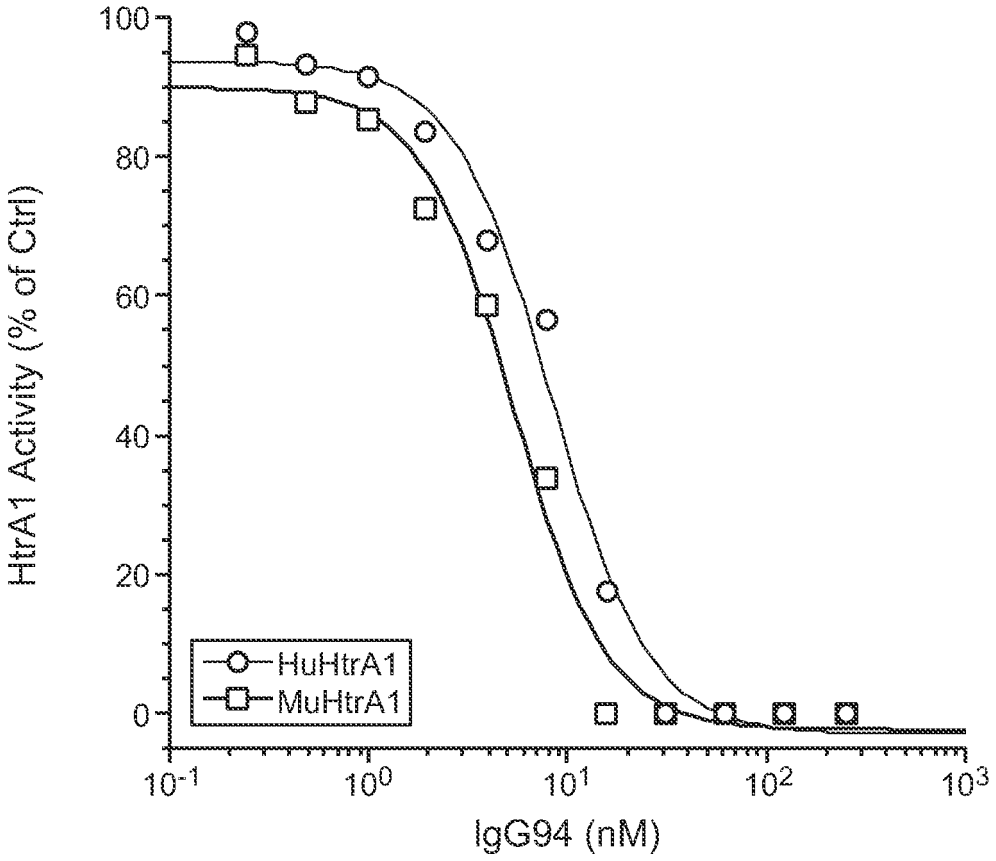

HtrA1 Activity (% of Ctrl)
100
80
60
40
20
0
HuHtrA1
MuHtrA1
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
IgG94 (nM)

FIG. 4

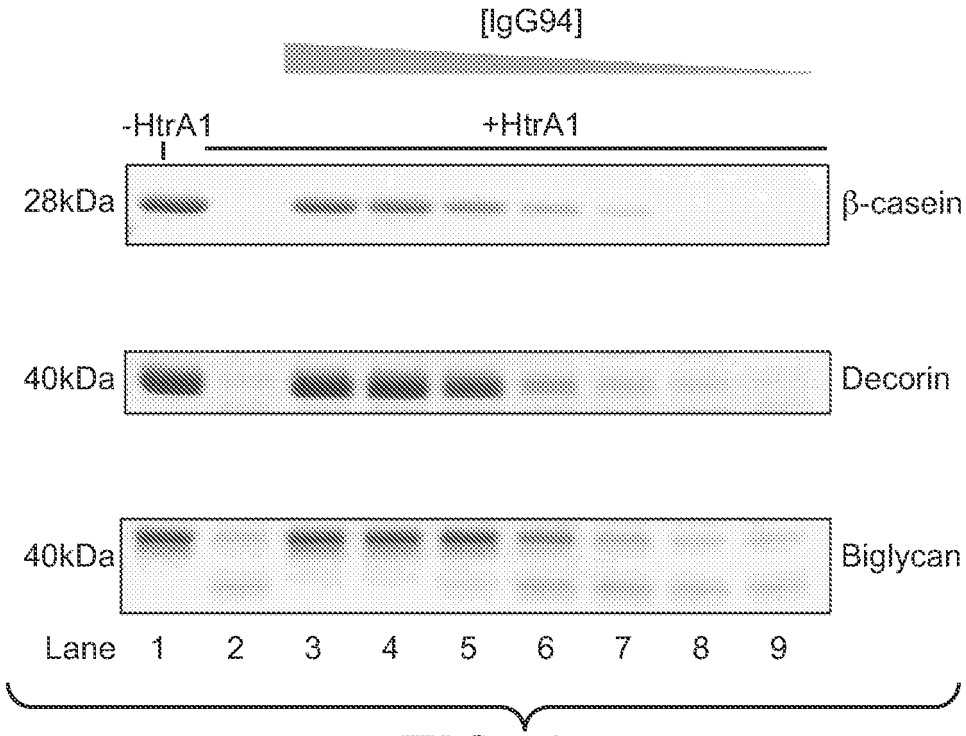
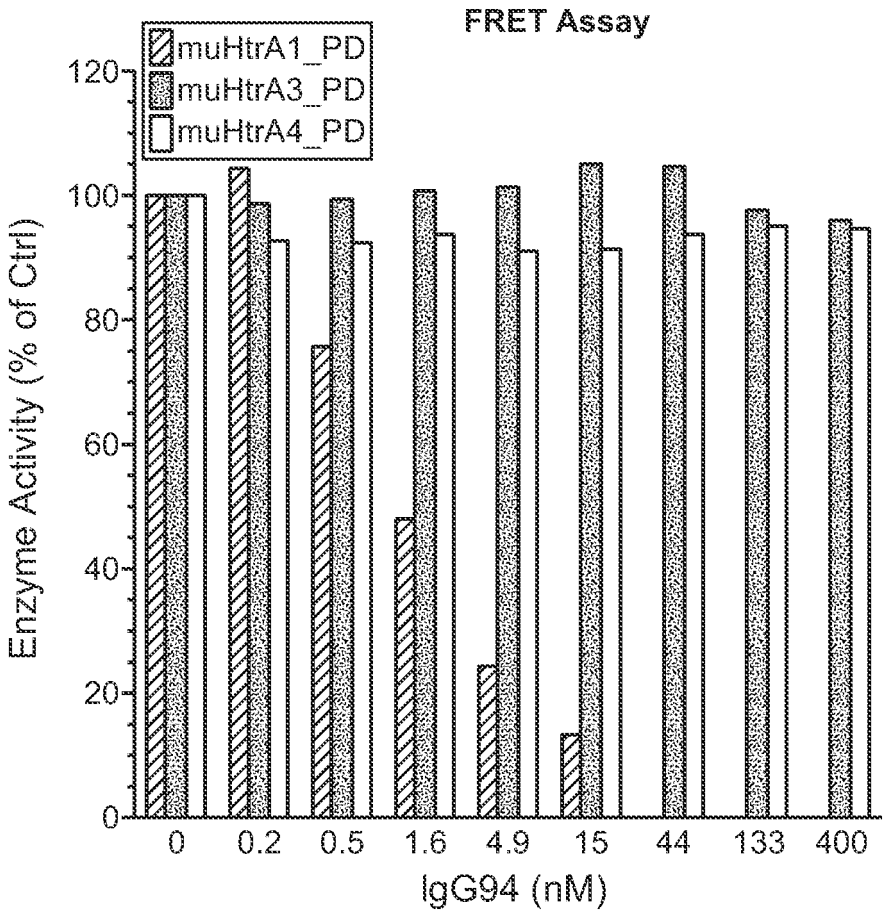
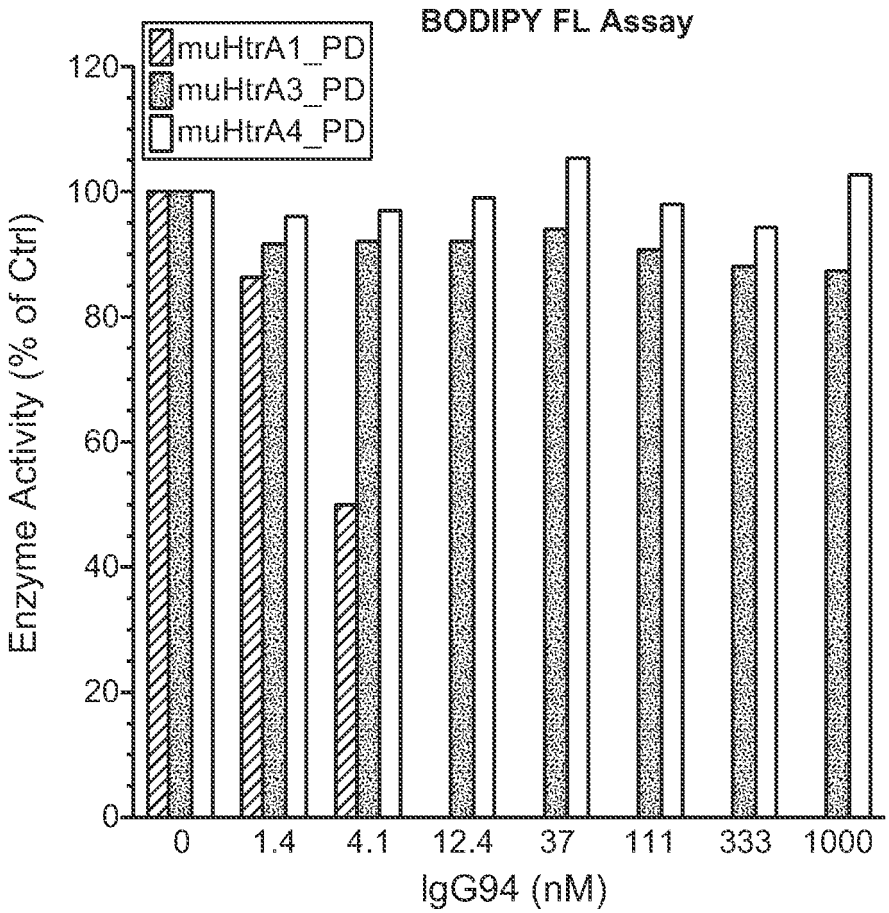

[IgG94]
-HtrA1
+HtrA1
28kDa
β-casein
40kDa
Decorin
40kDa
Biglycan
Lane 1 2 3 4 5 6 7 8 9

FIG. 6

FIG. 5


FRET Assay
muHtrA1_PD
muHtrA3_PD
muHtrA4_PD
Enzyme Activity (% of Ctrl)
120
100
80
60
40
20
0
0
0.2
0.5
1.6
4.9
15
44
133
400
IgG94 (nM)


BODIPY FL Assay
muHtrA1_PD
muHtrA3_PD
muHtrA4_PD
Enzyme Activity (% of Ctrl)
120
100
80
60
40
20
0
0
1.4
4.1
12.4
37
111
333
1000
IgG94 (nM)

HtrA1 Residue Number	YW505.94 Fab [EC50 (nM)] Mean ± SD	Relative to WT EC50 Fold Decrease
R190A	–	–
K191A	14.0 ± 3.3	2.5
V201A	112.5 ± 16.4	20
H220A	32.0 ± 1.4	5.7
T223A	62.9 ± 2.2	11.2
N224A	134.6 ± 12.3	24
K225A	52.2 ± 1.3	9.3
R227A	25.9 ± 0.2	4.6
E239A	5.4 ± 0.2	0.9
K241A	23.0 ± 0.5	4.1
K243A	64.9 ± 4.2	11.6
D244A	4.7 ± 0.3	0.8
E247A	41.7 ± 0.9	7.4
K248A	195.8 ± 21.9	35
D250A	9.4 ± 3.5	1.7
Y325A	7.7 ± 0.6	1.4
S328A	2.3 ± 0.3	0.4
L345A	–	–
WT	5.6 ± 0.9	1

FIG. 7A

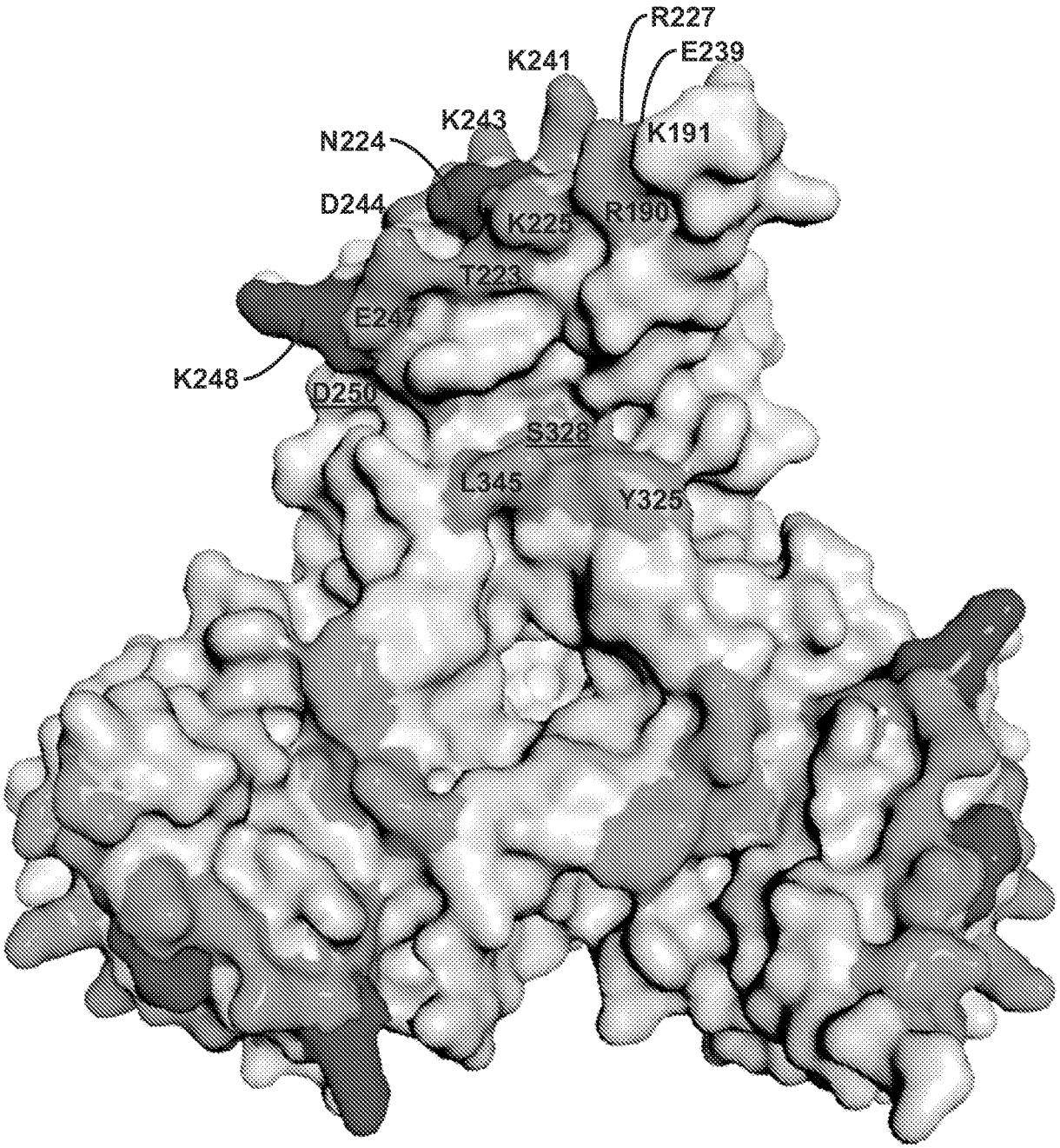

R227
E239
K241
K243
K191
N224
D244
K225
R190
T223
E247
K248
D250
S326
L345
Y325

FIG. 7B

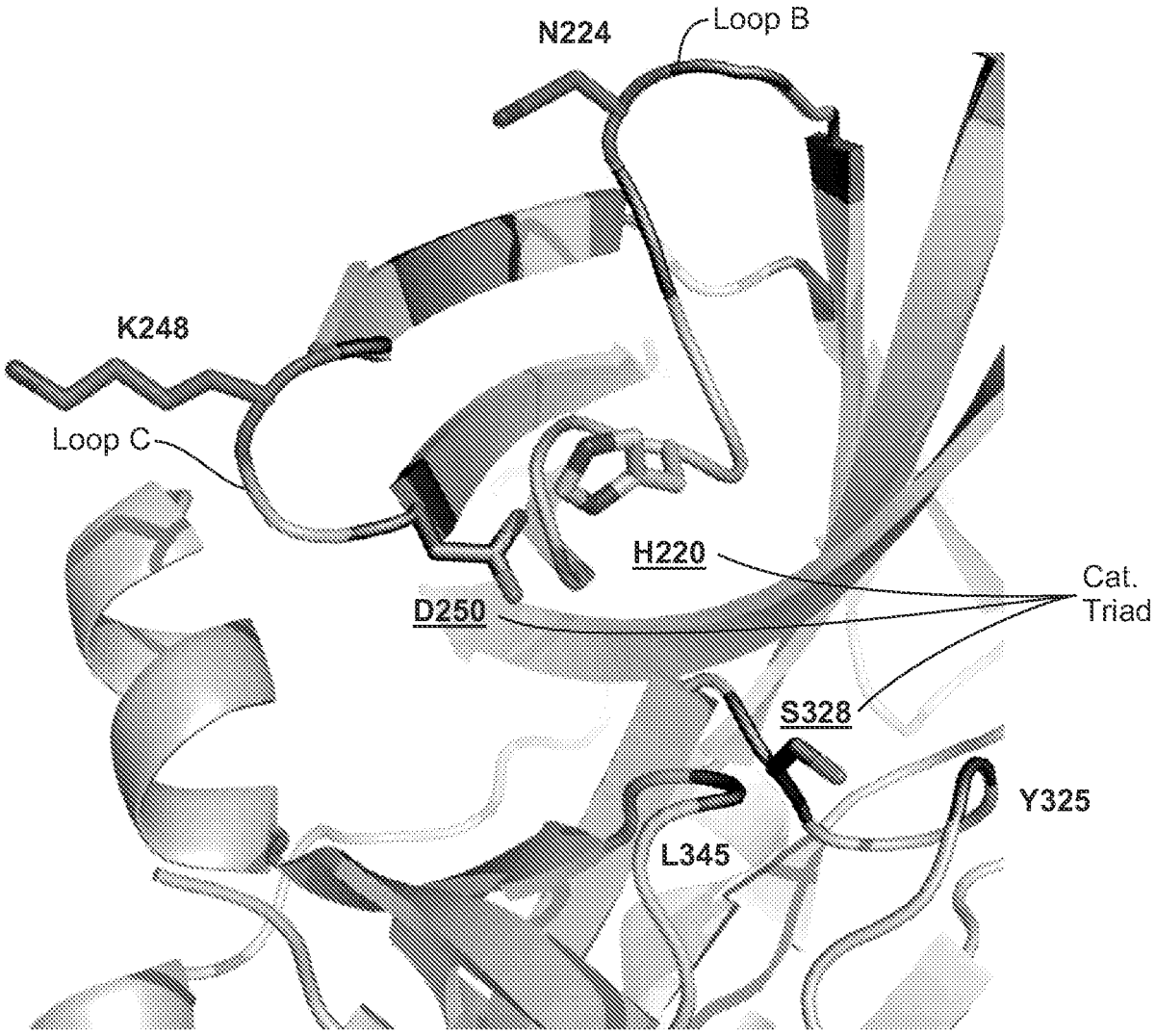


FIG. 7C

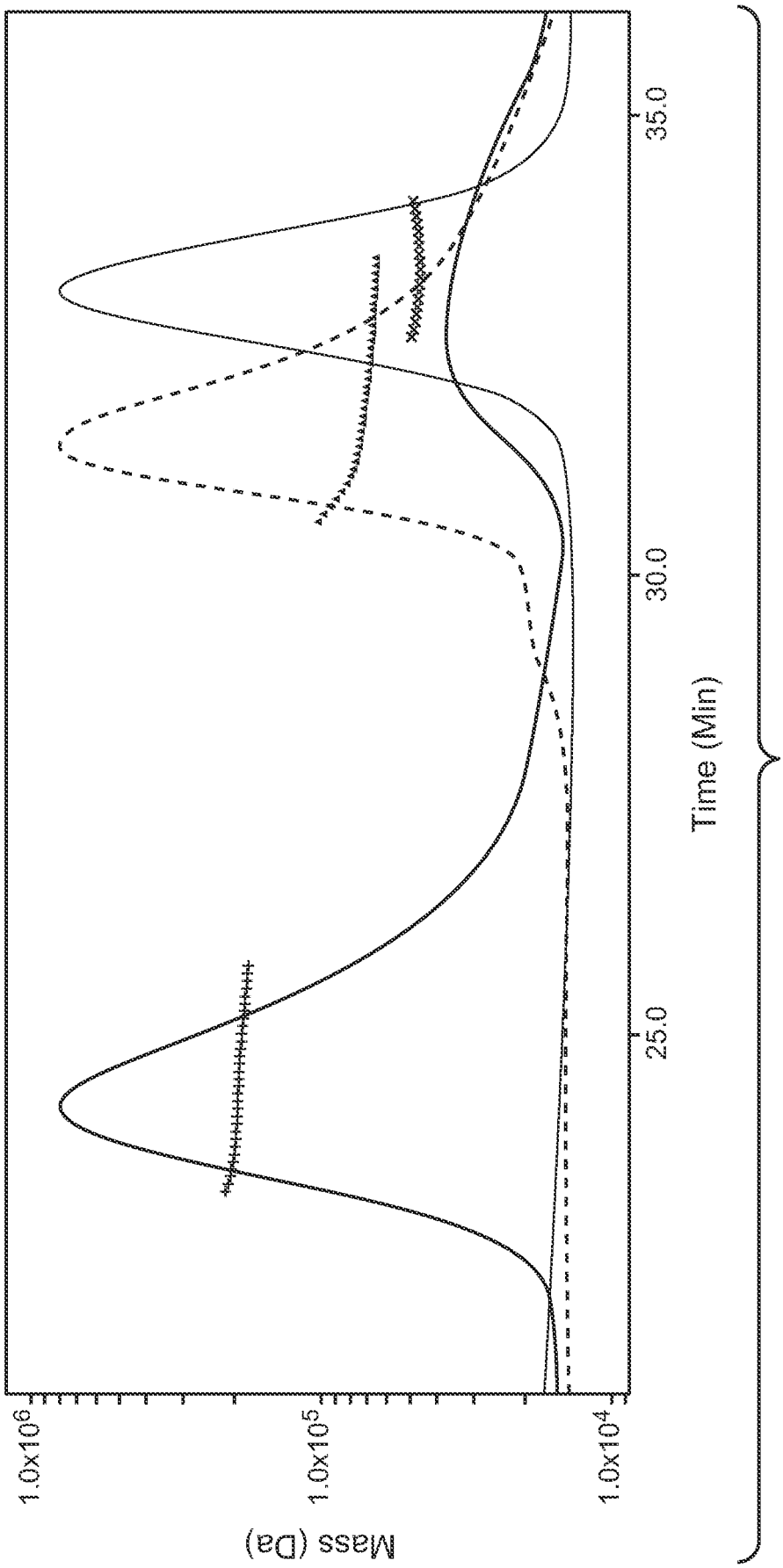

Fab94:HtrA1_PD
HtrA1_PD
Fab94
Mass (Da)
1.0x10^6
1.0x10^5
1.0x10^4
25.0
30.0
35.0
Time (Min)

FIG. 8A

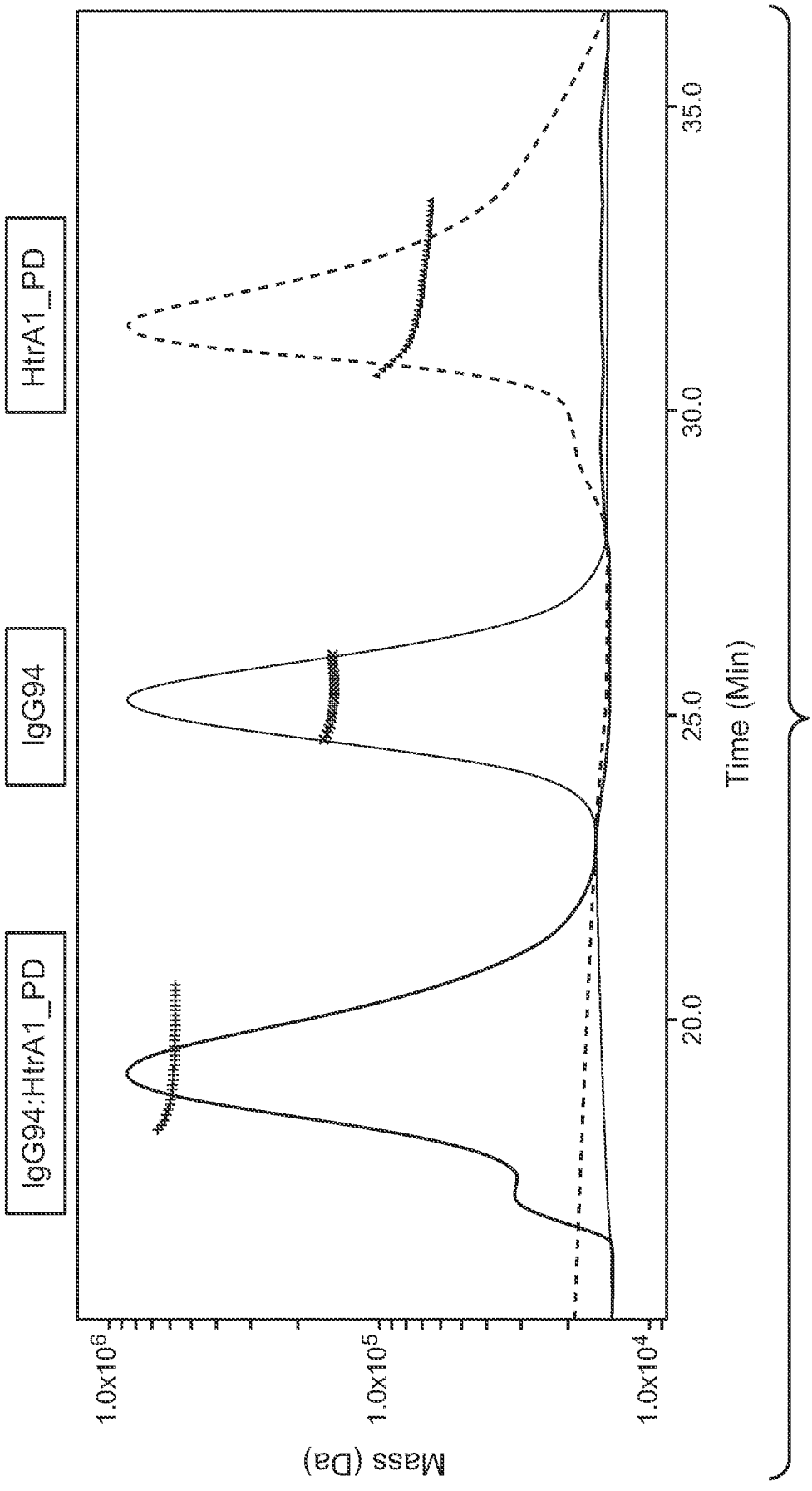

IgG94:HtrA1_PD
IgG94
HtrA1_PD
Mass (Da)
1.0x10^6
1.0x10^5
1.0x10^4
20.0
25.0
30.0
35.0
Time (Min)

FIG. 8B

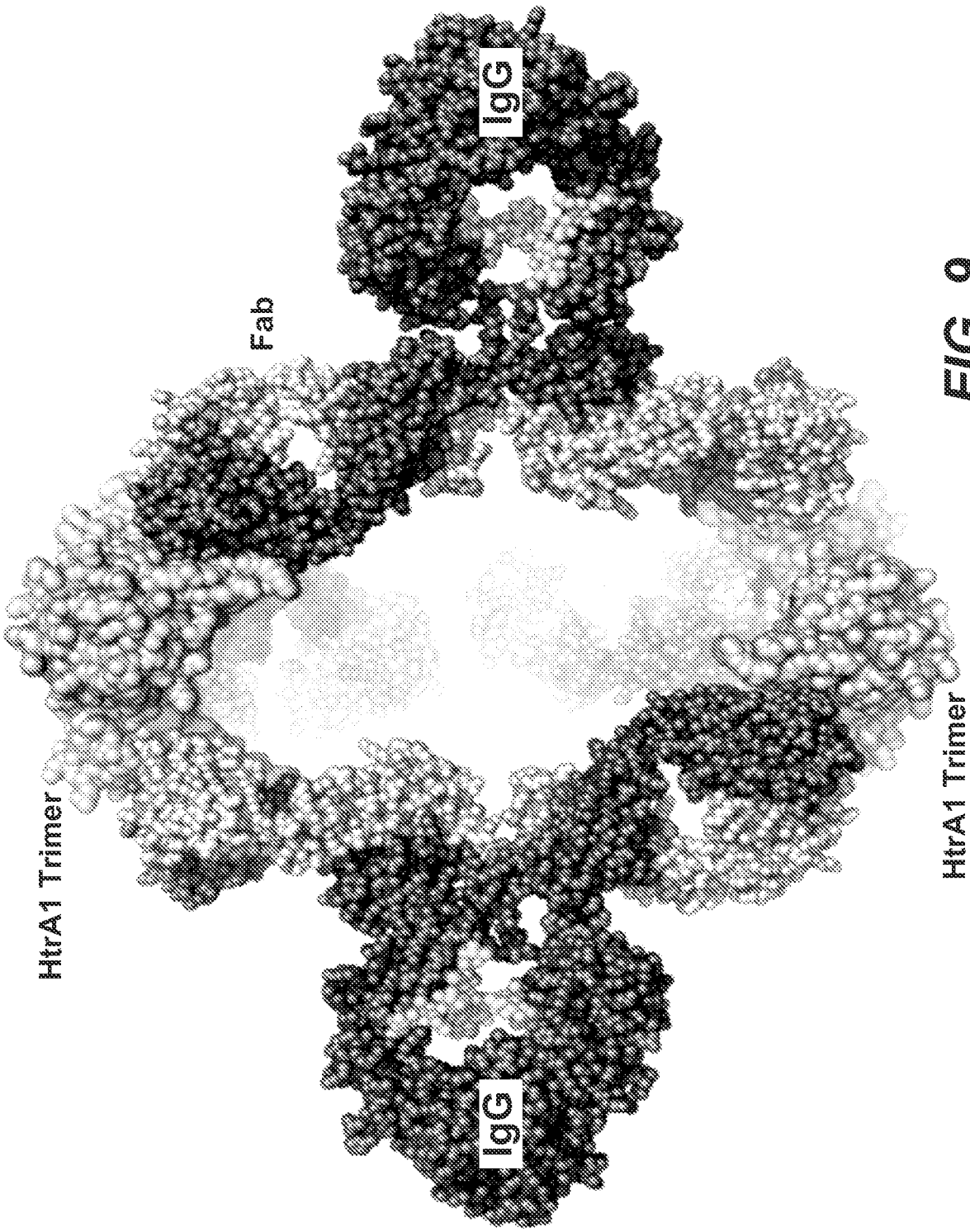


FIG. 9

```
huHtrA1          --MQIPRAALLPLLLLLLAAPASAQLSRAGRSAPLAAGCPDRCEPARCPPQPEHCEGGR- 57
muHtrA1          --MQSLRTTLLSLLLLLLAAPSLALPSGTGRSAPAATVCPEHCDPTRCAPPPTDCEGGR- 57
muHtrA3          --MQAR--ALLPATLAILATLAVLALARE-----PPAAPCPARCDVSRCPSP--RCPGGY- 49
muHtrA4          MSFQRLWAVRTQFLLLWLLLPAVPVPWAEARRSRVSLPCPDACDPTRCPTLPTCSAGLAP 60
                   :*    .     *  *   :             :  **  *: :**..    . *

huHtrA1          ARDACGCCEVCGAPEGAACG-LQEGPCGEGLQCVVPFGVPASATVRRRAQAGLCVCAS-- 114
muHtrA1          VRDACGCCEVCGALEGAACG-LQEGPCGEGLQCVVPFGVPASATVRRRAQAGLCVCAS-- 114
muHtrA3          VPDLCNCCLVCAASEGEPCGRPLDSPCGDSLECVR----------------GVCRCRW-- 91
muHtrA4          VPDRCGCCRVCAAAEGQECGGARGRPCAPRLRCGAPFSRDPSG----GAWLGTCGCAEGA 116
                 . * *.** **.* **  **     **.  *.*                  * * *

huHtrA1          -SEPVCGSDANTYANLCQLRAASRRSERLHRPPVIVLQRGACGQ-GQEDPNSLRHKYNFI 172
muHtrA1          -SEPVCGSDAKTYTNLCQLRAASRRSEKLRQPPVIVLQRGACGQ-GQEDPNSLRHKYNFI 172
muHtrA3          -THTVCGTDGHTYADVCALQAASRRALQVSGTPVRQLQKGACPS-GLHQLTSPRYKFNFI 149
muHtrA4          EDAVVCGSDGRTYPSLCALRKENRAARQRGALPAVPVQKGACEEAGTTRAGRLRRKYNFI 176
                     ***:*..**..:* *:  .* : :    *.  :*:*** . *       * *:***

huHtrA1          ADVVEKIAPAVVHIELFRKLPFSKREVPVASGSGFIVSEDGLIVTNAHVVTN------KH 226
muHtrA1          ADVVEKIAPAVVHIELYRKLPFSKREVPVASGSGFIVSEDGLIVTNAHVVTN------KN 226
muHtrA3          ADVVEKIAPAVVHIELFLRHPLFGRNVPLSSGSGFIMSEAGLIVTNAHVVSSSSTASGRQ 209
muHtrA4          AAVVEKVAPSVVHLQLFRRSPLTNQEIPSSSGSGFIVSEDGLIVTNAHVLTN------QQ 230
                 * ****:**:***::*: : *:  :::* :*******:** **********:.     ::

huHtrA1          RVKVELKNGATYEAKIKDVDEKADIALIKIDHQGKLPVLLLGRSSELRPGEFVVAIGSPF 286
muHtrA1          RVKVELKNGATYEAKIKDVDEKADIALIKIDHQGKLPVLLLGRSSELRPGEFVVAIGSPF 286
muHtrA3          QLKVQLQNGDAYEATIQDIDKKSDIATIVIHPKKKLPVLLLGHSADLRPGEFVVAIGSPF 269
muHtrA4          KIQVELQSGARYEATVKDIDHKLDLALIKIEPDTELPVLLLGRSSDLRAGEFVVALGSPF 290
                 :::*:*:.*  ***.::*:*.* *:* * *. . :*******:*::**.******:****
```

FIG. 10A

```
huHtrA1          SLQNTVTTGIVSTTQRGGKELGLRNSDMDYIQTDAIINYGNSGGPLVNLDGEVIGINTLK 346
muHtrA1          SLQNTVTTGIVSTTQRGGKELGLRNSDMDYIQTDAIINYGNSGGPLVNLDGEVIGINTLK 346
muHtrA3          ALQNTVTTGIVSTAQRDGKELGLRDSDMDYIQTDAIINYGNSGGPLVNLDGEVIGINTLK 329
muHtrA4          SLQNTVTAGIVSTTQRGGRELGLKNSDIDYIQTDAIINHGNSGGPLVNLDGDVIGINTLK 350
                 :******:*****:**.*:*****::**:**********:***********:********

huHtrA1          VTAGISFAIPSDKIKKFLTESHDRQAKGKAITKKKYIGIRMMSLTSSKAKELKDRHRDFP 406
muHtrA1          VTAGISFAIPSDKIKKFLTESHDRQAKGKAVTKKKYIGIRMMSLTSSKAKELKDRHRDFP 406
muHtrA3          VAAGISFAIPSDRITRFLSEFQNKHVKD---WKKRFIGIRMRTITPSLVEELKAANPDFP 386
muHtrA4          VTAGISFAIPSDRIRQFLEDYHERQLKGKAPLQKKYLGLRMLPLTLNLLQEMKRQDPEFP 410
                 *:***********:* :** : :::: *.    :*:::*:** .:* .  :*:*  . :**

huHtrA1          DVISGAYIIEVIPDTPAEAGGLKENDVIISINGQSVVSANDVSDVIKRESTLNMVVRRGN 466
muHtrA1          DVLSGAYIIEVIPDTPAEAGGLKENDVIISINGQSVVTANDVSDVIKKENTLNMVVRRGN 466
muHtrA3          AVSSGIYVQEVVPNSPSQRGGIQDGDIIVKVNGRPLADSSELQEAVLNESSLLLEVRRGN 446
muHtrA4          DVSSGVFVYEVIQGSAAASSGLRDHDVIVSINGQPVTTTTDVIEAVKDNDFLSIIVLRGS 470
                  * ** :: **: .:.:  .*::: *:*:.:**:.:. :.:: :.:  :. * : * **.

huHtrA1          EDIMITVIPEEIDP 480
muHtrA1          EDIVITVIPEEIDP 480
muHtrA3          DDLLFSIIPEVVM- 459
muHtrA4          QTLFLTVTPEIIN- 483
                 : :.::: ** :
```

FIG. 10B

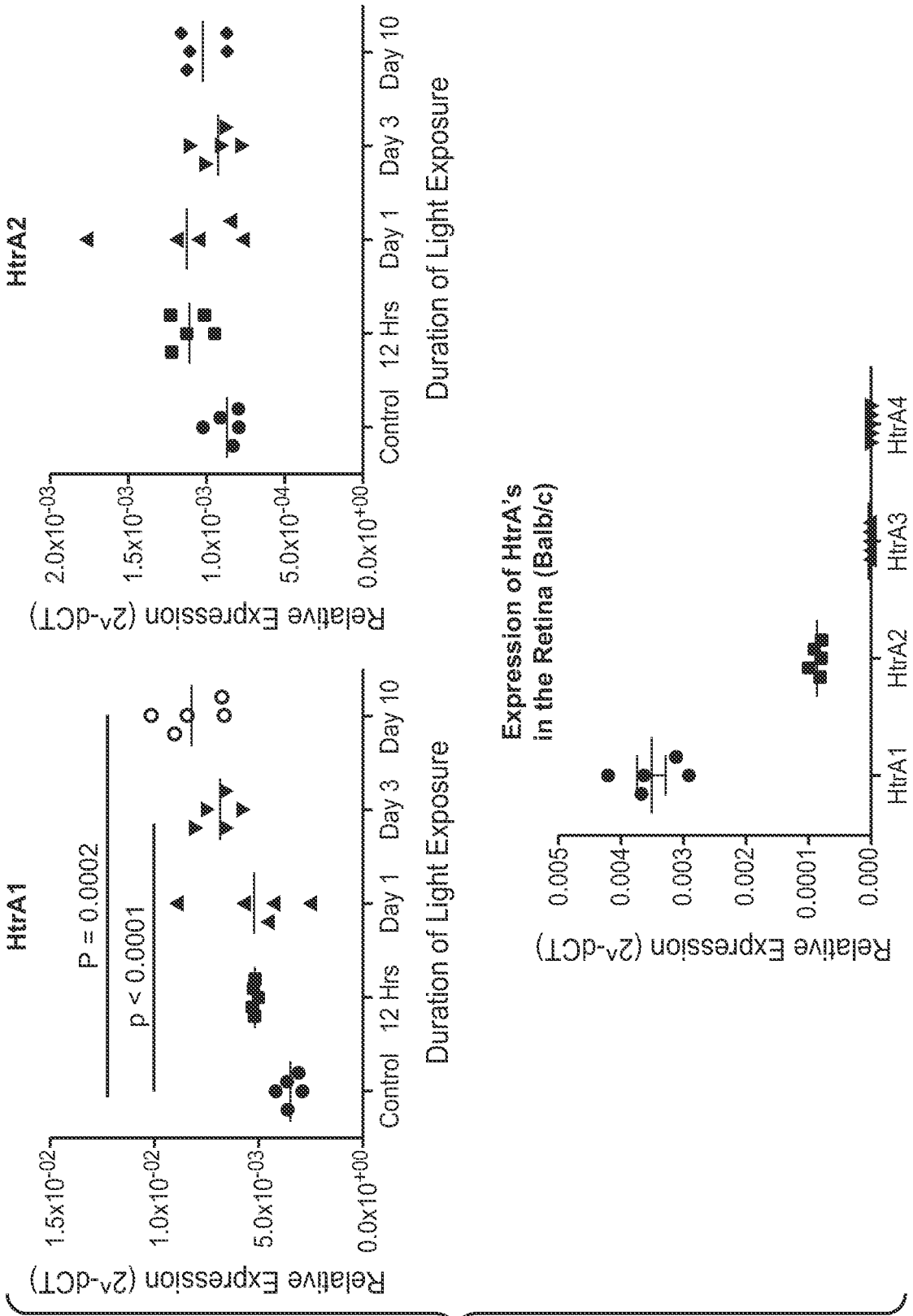

HtrA1
P = 0.0002
p < 0.0001
Relative Expression (2^-dCT)
1.5x10-02
1.0x10-02
5.0x10-03
0.0x10+00
Control
12 Hrs
Day 1
Day 3
Day 10
Duration of Light Exposure
HtrA2
Relative Expression (2^-dCT)
2.0x10-03
1.5x10-03
1.0x10-03
5.0x10-04
0.0x10+00
Control
12 Hrs
Day 1
Day 3
Day 10
Duration of Light Exposure
Expression of HtrA's in the Retina (Balb/c)
Relative Expression (2^-dCT)
0.005
0.004
0.003
0.002
0.0001
0.000
HtrA1
HtrA2
HtrA3
HtrA4

FIG. 11

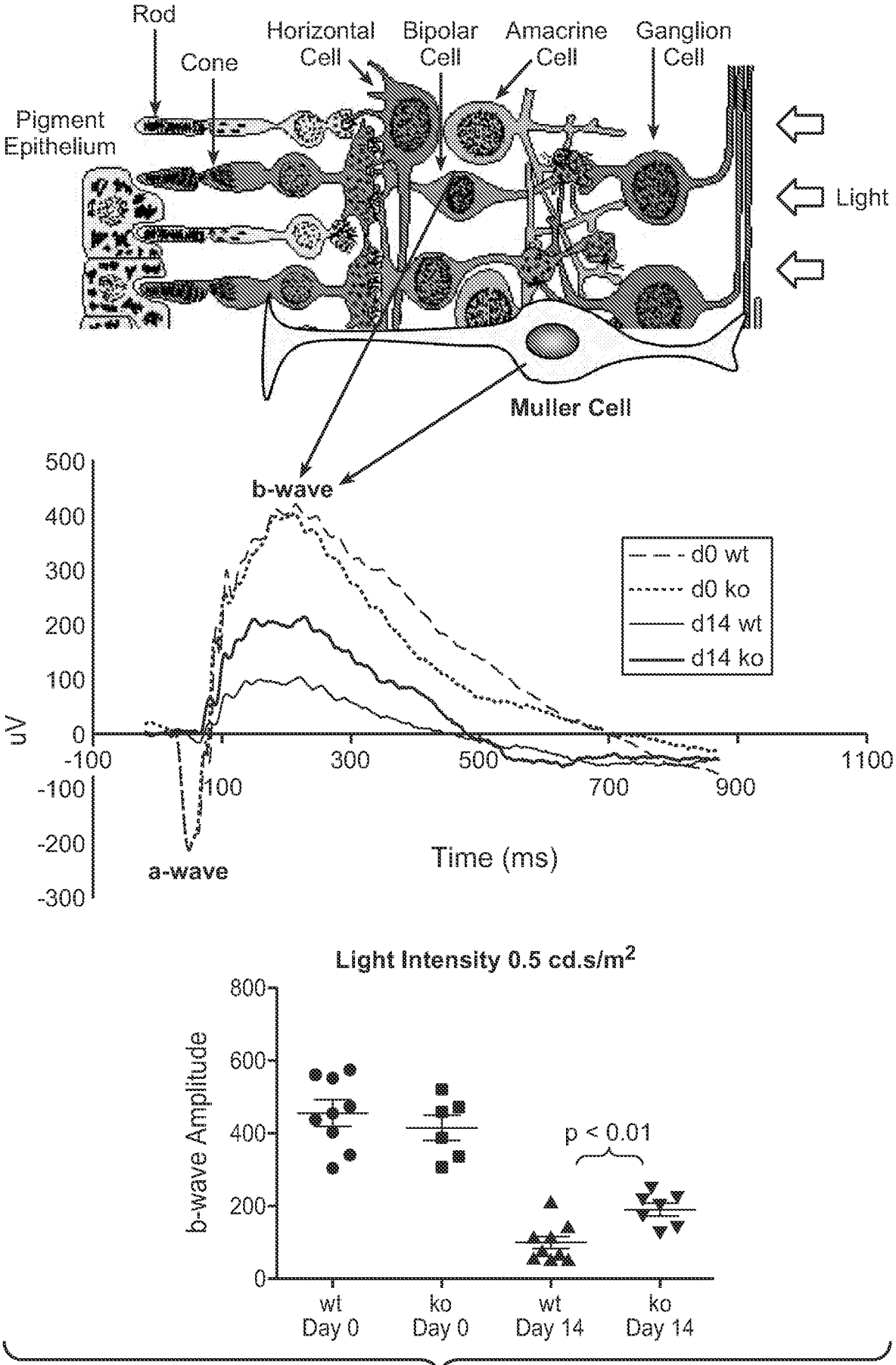

Rod
Cone
Horizontal Cell
Bipolar Cell
Amacrine Cell
Ganglion Cell
Pigment Epithelium
Light
Mullier Cell
b-wave
a-wave
uV
Time (ms)
d0 wt
d0 ko
d14 wt
d14 ko
Light Intensity 0.5 cd.s/m2
b-wave Amplitude
p < 0.01
wt Day 0
ko Day 0
wt Day 14
ko Day 14

FIG. 12

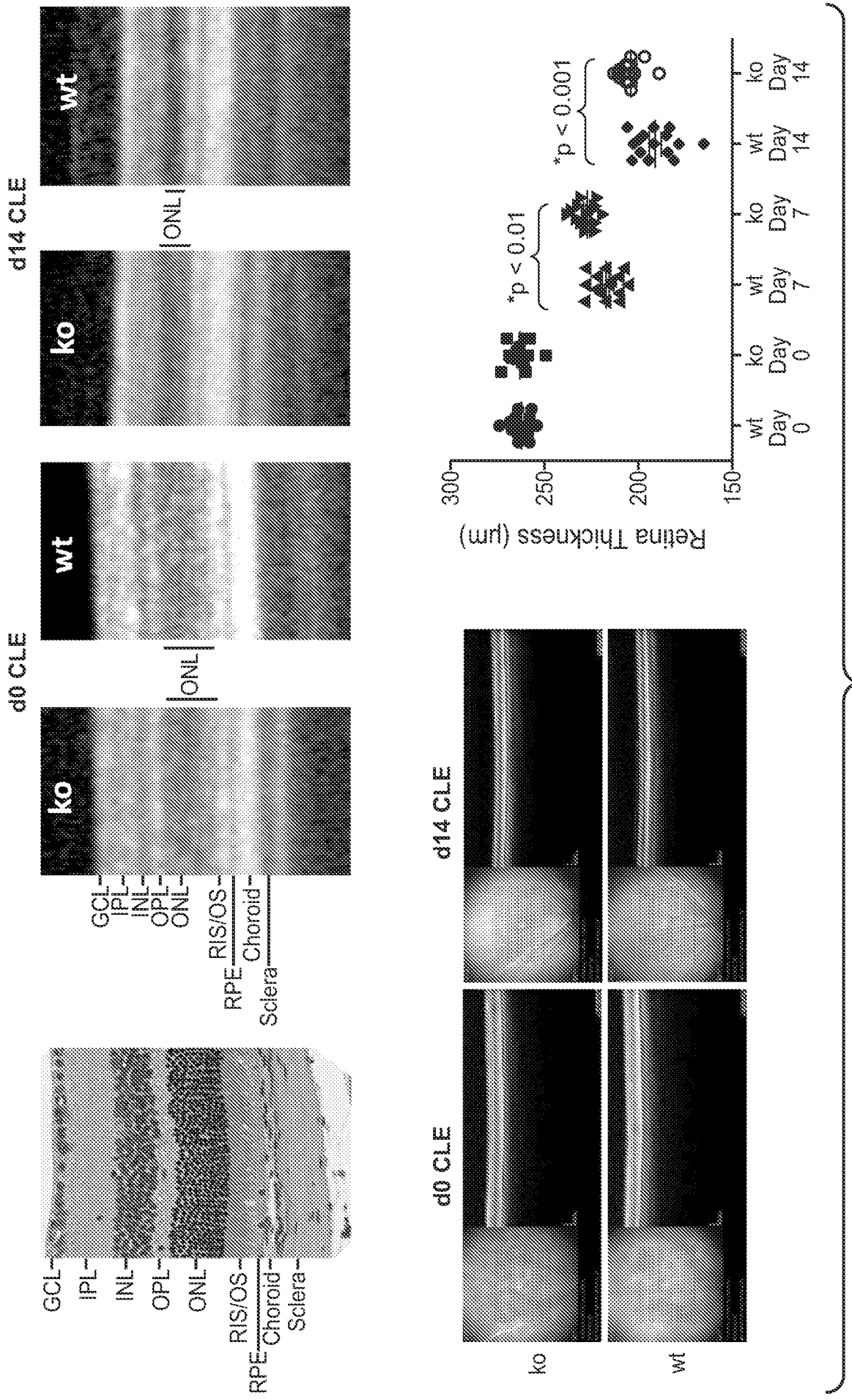

d0 CLE
d14 CLE
ko
wt
ONL
GCL
IPL
INL
OPL
ONL
RIS/OS
Choroid
RPE
Sclera
Retina Thickness (μm)
300
250
200
150
*p < 0.01
*p < 0.001
wt Day 0
ko Day 0
wt Day 7
ko Day 7
wt Day 14
ko Day 14

FIG. 13

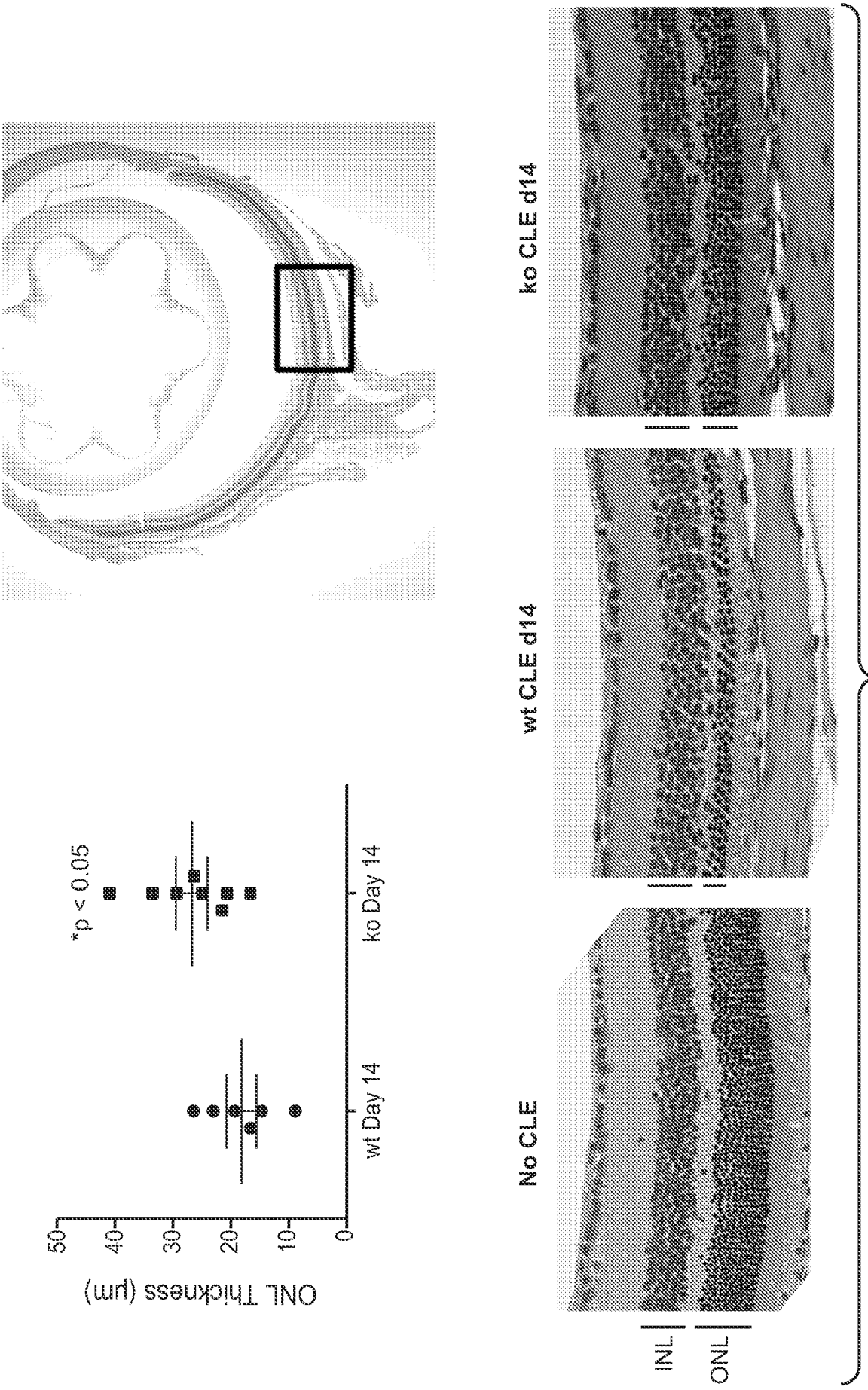

No CLE
wt CLE d14
ko CLE d14
INL
ONL
ONL Thickness (μm)
50
40
30
20
10
0
*p < 0.05
wt Day 14
ko Day 14

FIG. 14

Clone	CDR-L1						CDR-L2						CDR-L3						
	28	29	30	31	32	33	SEQ	50	51	52	53	54	55	SEQ	91	92	93	94	95	96	SEQ
YW505.94a (WT)	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	T	P	P	59
YW505.94a.1	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	V	Y	S	H	P	P	60
YW505.94a.7	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	N	P	P	61
YW505.94a.22	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	A	T	P	T	62
YW505.94a.26	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	T	P	P	59
YW505.94a.28	S	I	N	T	Y	L	55	S	A	S	F	L	Y	58	S	D	D	T	P	P	63
YW505.94a.37	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	S	S	P	A	64
YW505.94a.38	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	T	P	P	59
YW505.94a.39	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	V	Y	T	T	P	P	65
YW505.94a.40	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	V	Y	A	T	P	S	66
YW505.94a.42	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	N	S	P	A	67
YW505.94a.46	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	S	T	P	A	68
YW505.94a.47	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	T	P	P	59
YW505.94a.50	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	A	P	T	69
YW505.94a.51	D	V	G	T	Y	L	56	S	A	S	F	L	Y	58	D	S	T	L	P	P	70
YW505.94a.52	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	D	A	A	P	P	71
YW505.94a.54	V	V	G	N	Y	L	57	S	A	S	F	L	Y	58	S	D	D	H	P	P	72
YW505.94a.77	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	T	P	P	59
YW505.94a.78	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	S	T	P	P	73
YW505.94a.82	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	T	P	P	59
YW505.94a.89	D	V	S	T	A	V	54	S	A	S	F	L	Y	58	S	Y	T	R	P	P	74

FIG. 15

Clone	CDR-H1							CDR-H2								CDR-H3								
	26	27	28	29	30	31	32	33	SEQ	50	51	52	A	53	54	55	56	57	58	SEQ	95	96	97	98	99	100	A	B	C	D	SEQ
YW505.94a (WT)	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.1	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.7	G	F	S	I	S	D	Y	Y	76	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.22	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.26	G	F	S	I	D	G	Y	Y	77	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.28	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.37	G	F	S	I	S	D	Y	Y	76	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.38	G	F	T	I	Y	D	Y	Y	78	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.39	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.40	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.42	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	D	82	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.46	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	T	W	G	H	Y	84
YW505.94a.47	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	D	82	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.50	G	F	S	I	S	D	Y	Y	76	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.51	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.52	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.54	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.77	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	T	W	G	H	Y	84
YW505.94a.78	G	F	S	I	A	G	Y	Y	79	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.82	G	F	T	I	S	D	Y	Y	80	W	I	D	P	Y	G	G	D	T	N	81	G	T	F	L	T	S	W	G	H	Y	83
YW505.94a.89	G	F	S	I	S	G	Y	Y	75	W	I	D	P	Y	G	G	D	T	D	82	G	T	F	L	T	S	W	G	H	Y	83

FIG. 16

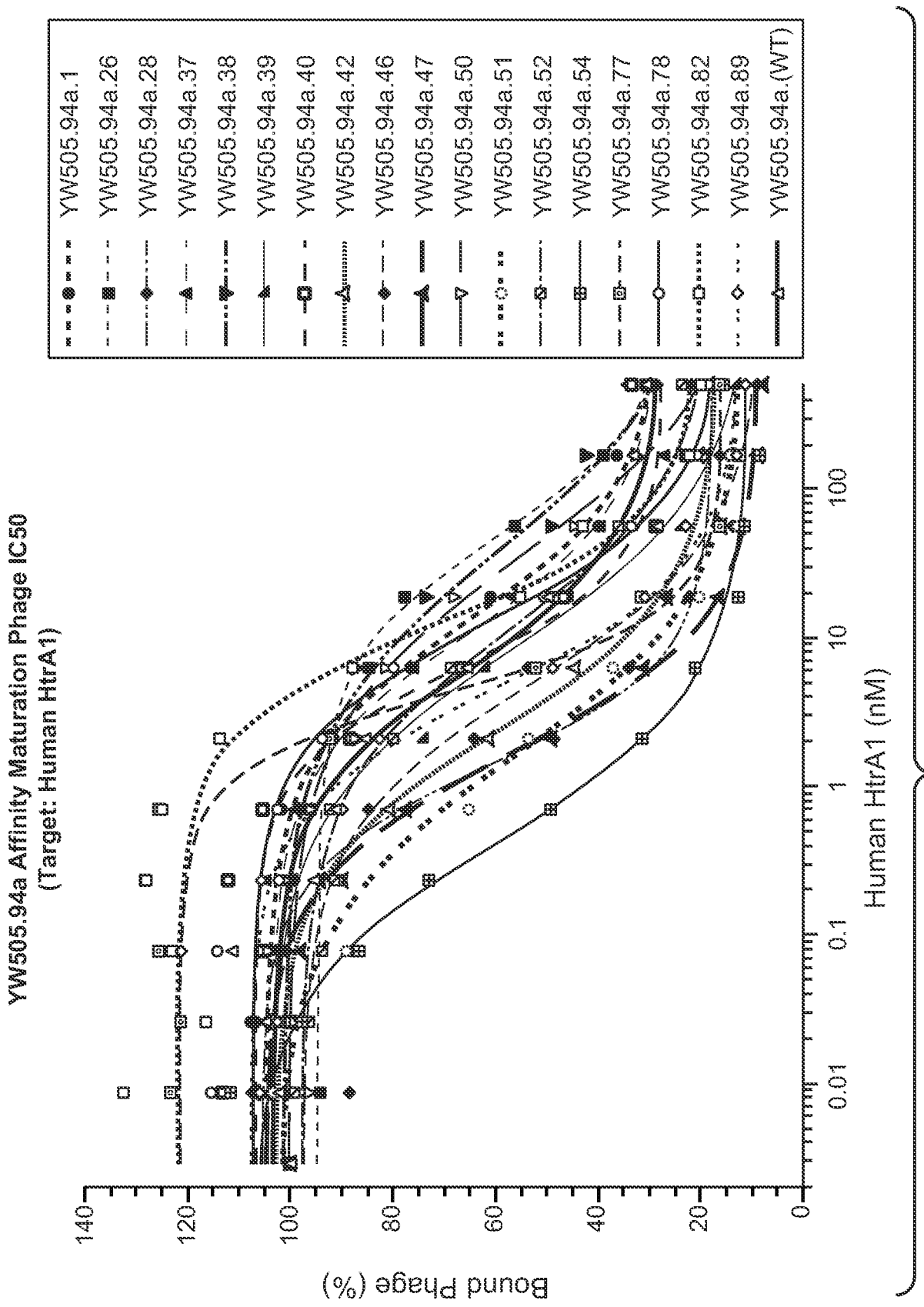

YW505.94a Affinity Maturation Phage IC50
(Target: Human HtrA1)
YW505.94a.1
YW505.94a.26
YW505.94a.28
YW505.94a.37
YW505.94a.38
YW505.94a.39
YW505.94a.40
YW505.94a.42
YW505.94a.46
YW505.94a.47
YW505.94a.50
YW505.94a.51
YW505.94a.52
YW505.94a.54
YW505.94a.77
YW505.94a.78
YW505.94a.82
YW505.94a.89
YW505.94a.(WT)
Bound Phage (%)
0
20
40
60
80
100
120
140
Human HtrA1 (nM)
0.01
0.1
1
10
100

FIG. 17

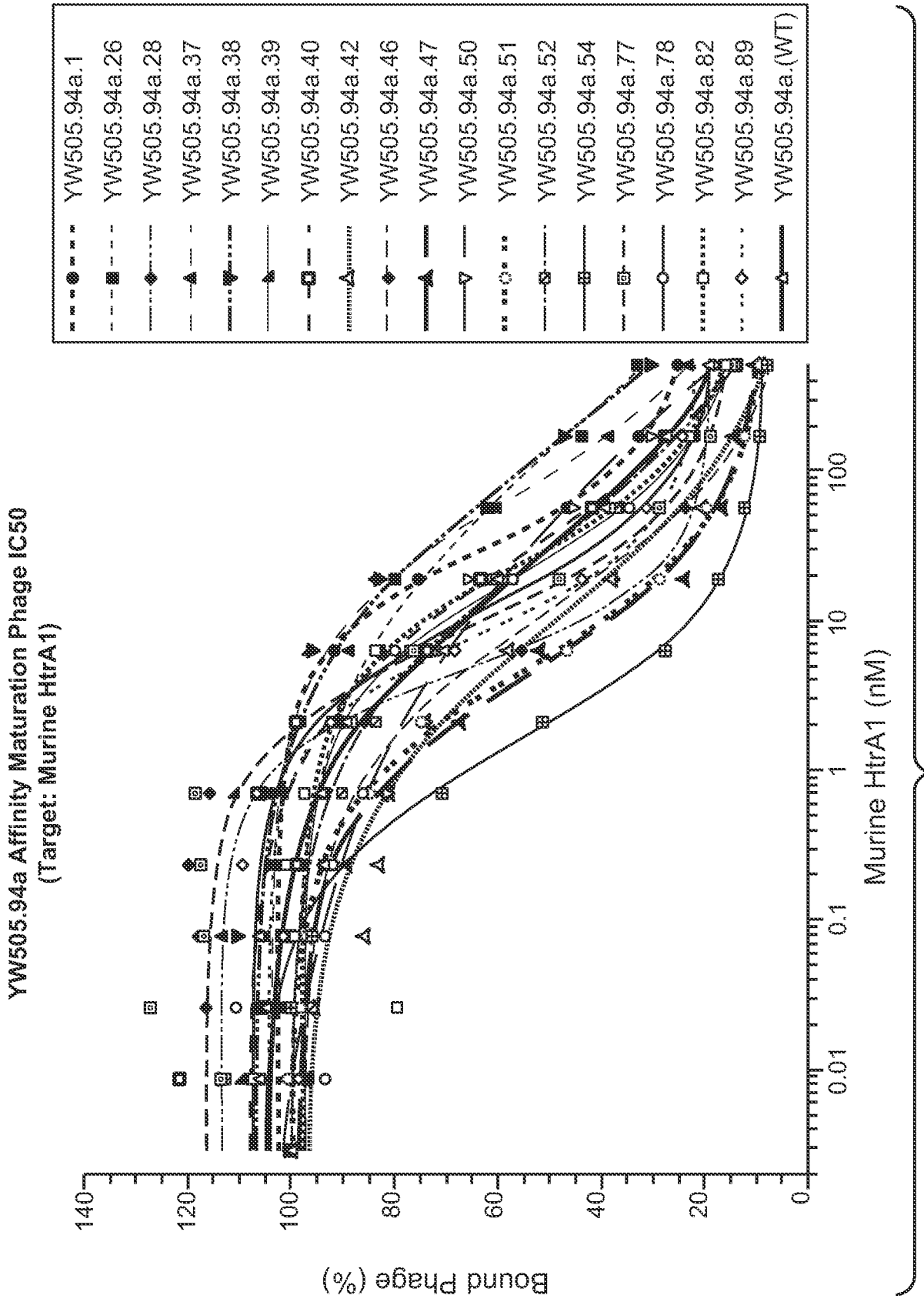

YW505.94a Affinity Maturation Phage IC50
(Target: Murine HtrA1)
Bound Phage (%)
Murine HtrA1 (nM)
0
20
40
60
80
100
120
140
0.01
0.1
1
10
100
YW505.94a.1
YW505.94a.26
YW505.94a.28
YW505.94a.37
YW505.94a.38
YW505.94a.39
YW505.94a.40
YW505.94a.42
YW505.94a.46
YW505.94a.47
YW505.94a.50
YW505.94a.51
YW505.94a.52
YW505.94a.54
YW505.94a.77
YW505.94a.78
YW505.94a.82
YW505.94a.89
YW505.94a.(WT)

FIG. 18

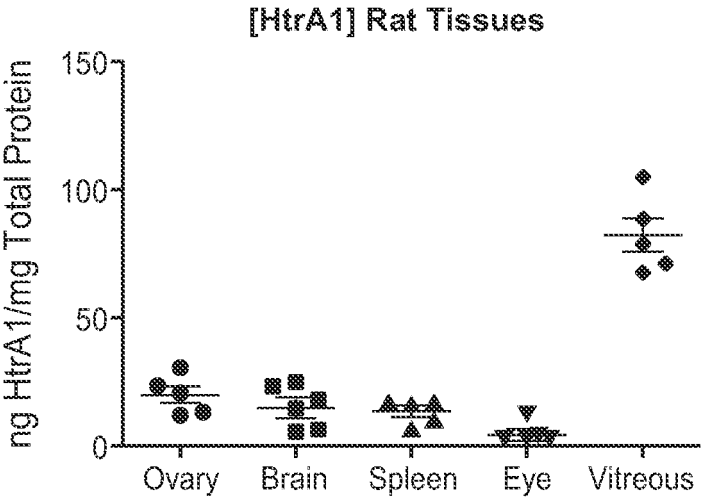


FIG. 19A

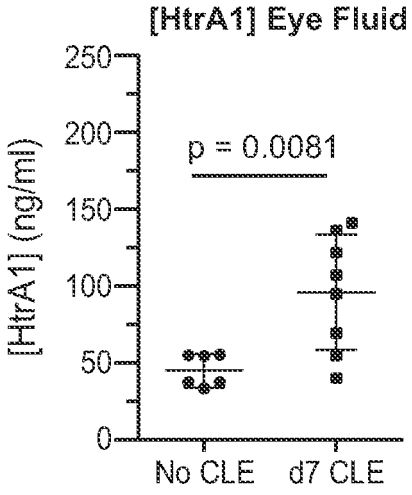


FIG. 19B

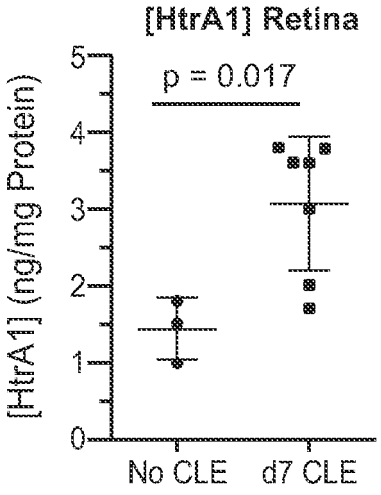


FIG. 19C