FIGURE 1

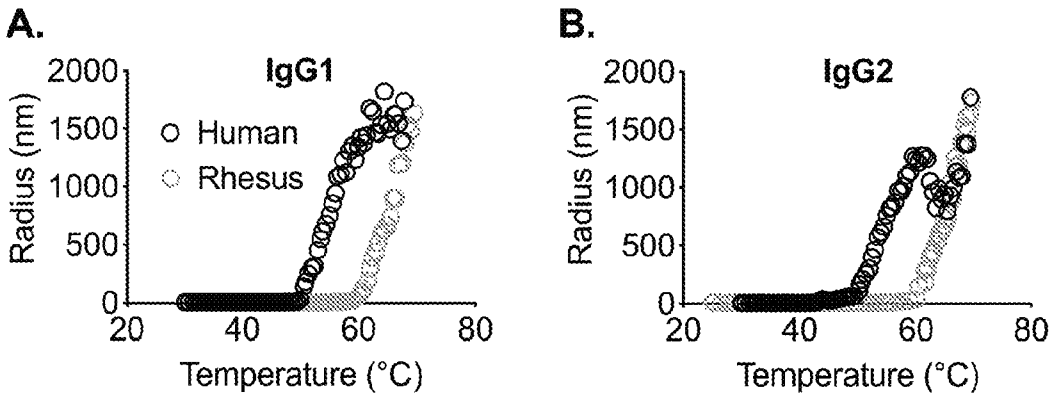

A.
IgG1
Human
Rhesus
Radius (nm)
2000
1500
1000
500
0
20
40
60
80
Temperature (°C)
B.
IgG2
Radius (nm)
2000
1500
1000
500
0
20
40
60
80
Temperature (°C)

FIGURE 2

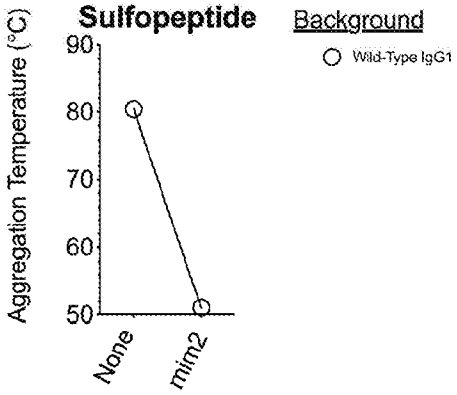

Sulfopeptide
Background
Wild-Type IgG1
Aggregation Temperature (°C)
90
80
70
60
50
None
mim2

FIGURE 3

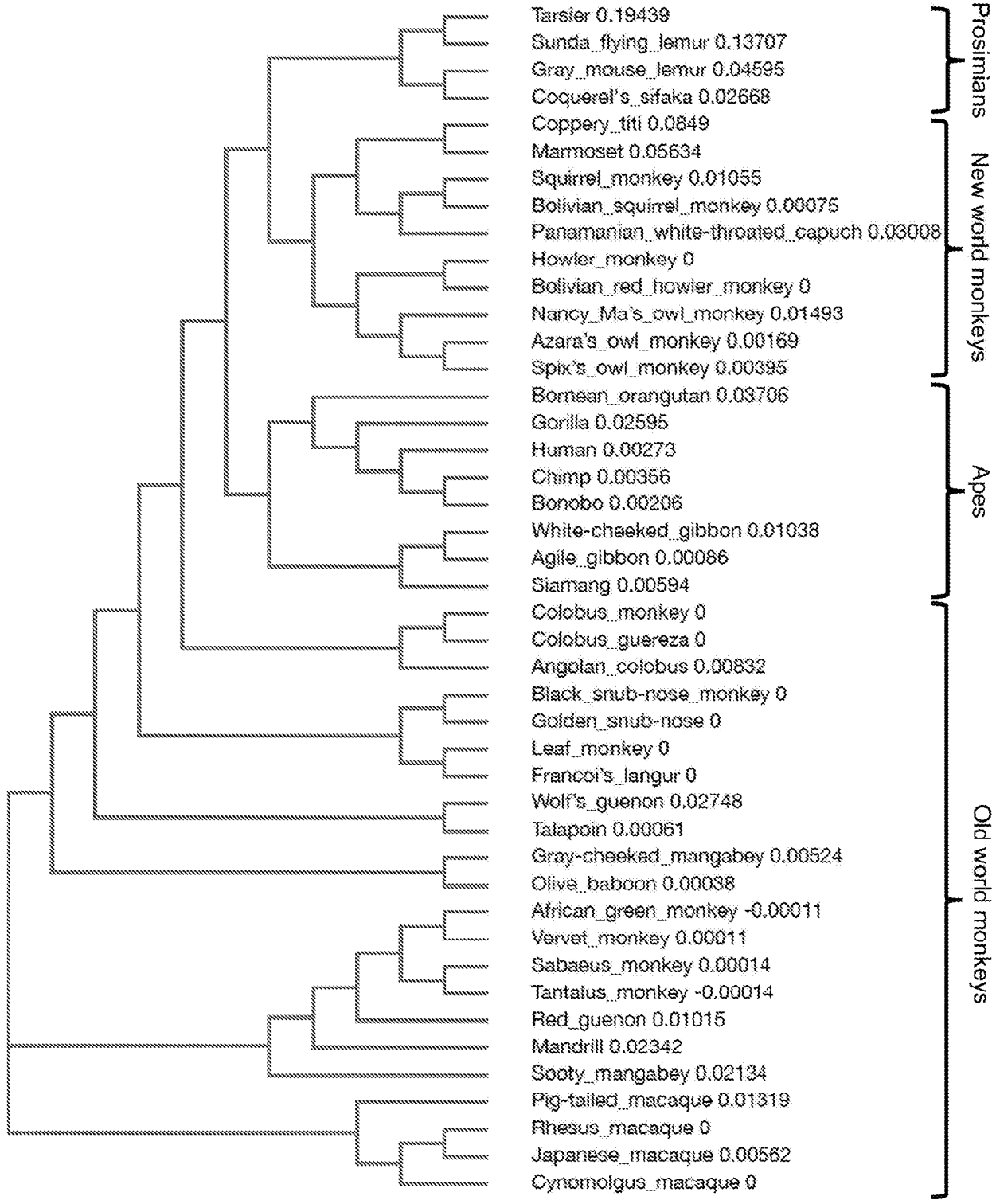

Tarsier 0.19439
Sunda_flying_lemur 0.13707
Gray_mouse_lemur 0.04595
Coquerel's_sifaka 0.02668
Coppery_titi 0.0849
Marmoset 0.05634
Squirrel_monkey 0.01055
Bolivian_squirrel_monkey 0.00075
Panamanian_white-throated_capuch 0.03008
Howler_monkey 0
Bolivian_red_howler_monkey 0
Nancy_Ma's_owl_monkey 0.01493
Azara's_owl_monkey 0.00169
Spix's_owl_monkey 0.00395
Bornean_orangutan 0.03706
Gorilla 0.02595
Human 0.00273
Chimp 0.00356
Bonobo 0.00206
White-cheeked_gibbon 0.01038
Agile_gibbon 0.00086
Siamang 0.00594
Colobus_monkey 0
Colobus_guereza 0
Angolan_colobus 0.00832
Black_snub-nose_monkey 0
Golden_snub-nose 0
Leaf_monkey 0
Francoi's_langur 0
Wolf's_guenon 0.02748
Talapoin 0.00061
Gray-cheeked_mangabey 0.00524
Olive_baboon 0.00038
African_green_monkey -0.00011
Vervet_monkey 0.00011
Sabaeus_monkey 0.00014
Tantalus_monkey -0.00014
Red_guenon 0.01015
Mandrill 0.02342
Sooty_mangabey 0.02134
Pig-tailed_macaque 0.01319
Rhesus_macaque 0
Japanese_macaque 0.00562
Cynomolgus_macaque 0
Prosimians
New world monkeys
Apes
Old world monkeys

FIGURE 4

A.

	10s	20s	30s	40s	50s
Apes	12345678901234567890123456789012345678901234--3456789012345678				
Human	KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGS--FLTKGPSKLNDRADSR				
Chimp	KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQTKILGNQGS--FLTKGPSKLNDRVDSR				
Bonobo	KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQTKILGNQGS--FLTKGPSKLNDRVDSR				
Gorilla	NKVVLGKKGDTVELNCTASQKKSIQFHWKNSNQMKILGNQGS--FLTKGPSKLSDRADSR				
Bornean orangutan	KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQTKILGNQGS--FLTKGPSKLSNRADSR				
White-cheeked gibbon	KKVVLGKKGDTVELTCTASPKKSIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Agile gibbon	KKVVLGKKGDTVELTCTASPKKSIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Siamang	KKVVLGKKGDTVELTCIASPKKSIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				

	10s	20s	30s	40s	50s
Old World Monkeys	12345678901234567890123456789012345678901234--3456789012345678				
Colobus monkey	KNVVLGKKGDTVELTCNAPSKKNIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Colobus guereza	KNVVLGKKGDTVELTCNAPSKKNIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Angolan colobus	KNVVLGKKGDTVELTCNAPPKKNIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
African green monkey	XXVVLGKKGDTVELTCNASQKTTTQFHWKNSNQTKILGKQGS--FLTKGSSKLRDRIDSR				
Vervet monkey	KKVVLGKKGDTVELTCNASQKTTTQFHWKNSNQTKILGKQGS--FLTKGSSKLRDRIDSR				
Sabaeus monkey	KKVVLGKKGDTVELTCNASQNTTTQFHWKNSNQIKILGKQGS--FLTKGSSKLRDRIDSR				
Tantalus monkey	XXVVLGKKGDTVELTCNASQNTTTQFHWKNSNQIKILGKQGS--FLTKGSSKLRDRIDSR				
Red guenon	XXVVLGKKGDTVELTCNASQKTTTQFHWKNSNQMKILGKQGS--FLTKGPSKLRDRTDSR				
Sooty mangabey	KNVVLGKKGDTVELACNASQKKSTQFHWKNSKQIKILGNQGS--FLTKGSSKLSDRADSR				
Mandrill	KNVVLGKKGDTVELTCNASQKKNTPFHWKNSKQIKILGKQSS--FLTKGPSKLSDRIDSR				
Black snub-nose monkey	KKVVLGKKGDTVELTCSASQKKNIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Golden snub-nose	KKVVLGKKGDTVELTCSASQKKNIQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Leaf monkey	KKVVLGKKGDTVELTCSASQKKNIQFHWKNSKQIKILGNQGS--FLTKGPSKLSDRADSR				
Francoi's langur	KKVVLGKKGDTVELTCSASQKKNIQFHWKNSKQIKILGNQGS--FLTKGPSKLSDRADSR				
Pig-tailed macaque	KKVVLGKKGDTVELTCNASQKKNTQFHWKNSDQIKILGIQGS--FLTKGPSKLSDRADSR				
Rhesus macaque	KKVVLGKKGDTVELTCNASQKKNTQFHWKNSNQIKILGIQGS--FLTKGPSKLSDRADSR				
Cynomolgus macaque	KKVVLGKKGDTVELTCNASQKKNTQFHWKNSNQIKILGIQGS--FLTKGPSKLSDRADSR				
Japanese macaque	KKVVLGKKGDTVELTCNASQKKNTQFHWKNSNQIKILGIQGS--FLTKGPSKLSDRADSR				
Wolf's guenon	KKVVLGKKGGTVELTCNATQKKNTQFHWKHSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Talapoin	KKVVLGKKGDTVELTCNASQKKNTQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Gray-cheeked mangabey	KKVVLGKKGDTVELTCNASQKKSTQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				
Olive baboon	KKVVLGKKGDTVELTCNASQKKSTQFHWKNSNQIKILGNQGS--FLTKGPSKLSDRADSR				

	10s	20s	30s	40s	50s
New World Monkeys	12345678901234567890123456789012345678901234--3456789012345678				
Coppery titi	KTVVLGKKGETVELSCETSLKKTLQFYWKTSDQIKILGIQGF--LLTKGQSKLADRIDSK				
Marmoset	KTVVLGKKGEMVELPCETSLKKKLQFHWKTSNQIKILGIQGS--FVTKGQSKLANRIDSK				
Squirrel monkey	KTVVLGKKGEVVELPCETSLKKNVPFHWKTSDRIKILGVQNY--FVTRGQSKLTDRIDSK				
Bolivian squirrel monkey	KTVVLGKKGEVVELPCETSLKKNVPFHWKTSDQIKILGVQNY--FVTRGQSKLTDRIDSK				
Howler monkey	KTVVLGRKGETVELSCETSPKKNLQFHWKTSNQIKILGVQGS--SLTKGQSKLADRIDSK				
Bolivian red howler monkey	KTVVLGRKGETVELSCETSPKKNLQFHWKTSNQIKILGVQGS--SLTKGQSKLADRIDSK				
Panamanian white-throated capuchin	KTVVLGKKGEMVELPCETSLKKNTQFHWKTSDQIKILGIQNS--FLTRGQSKLADRIDSK				
Nancy Ma's owl monkey	KTVVLGEKGETVELPCETSLKKNVQFHWKTSDQIKILGNQGS--FLTRGQSKLADRIDSK				
Azara's owl monkey	KTVVLGEKGETVELPCETSLKKNVQFHWKTSDQIKILGNQGS--FLTRGQSKLADRIDSK				
Spix's owl monkey	KTVVLGEKGETVELPCETSLKKNVQFHWKTSDQIKILGIQGS--FLTRGQSKLADRIDSK				

	10s	20s	30s	40s	50s
Prosimians	12345678901234567890123456789012345678901234--3456789012345678				
Tarsier	KEVVLAKKGETGELPCQGSPKKSMSFSWKYSNQVMILRNQGS--FWITGSSRLKPRVESK				
Sunda flying lemur	KEVILGKKGDMVELPCKASEKRYLLFSWKHSDQIKILGNQGS--FWITGSSKLKHRVESR				
Gray mouse lemur	KEVVLGRKGDTVELPCKASQKKAIPFAWKHSNQTRILGKQGSSSFETTGPSMMKNRVESK				
Coquerel's sifaka	KEVVLGRKGDTVELPCKASQKKSMPFAWKHSNQTRILGKQGSSYFETTGPSMMKNRVESK				

B.

```
                                    60s       70s       80s       90s       100s      110s
Apes                                901234567890123456789012345678901234567890123456789012345678
Human                               RSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLTL
Chimp                               RSLWDQGNFTLIIKNLKIEDSDTYICEVGDQKEEVQLLVFGLTANSDTHLLQGQSLTLTL
Bonobo                              RSLWDQGNFPLIIKNLKIEDSDTYICEVGDQKEEVQLLVFGLTANSDTHLLQGQSLTLTL
Gorilla                             RSLWDQGNFPLIIKNLKIEDSDTYICEVEGQKEEVQLLVFGLTANSDTHLLQGQSLTLTL
Bornean orangutan                   RSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLAL
White-cheeked gibbon                KSLWDQRNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLTL
Agile gibbon                        KSLWDQRNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLTL
Siamang                             KSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLTL

                                    60s       70s       80s       90s       100s      110s
Old World Monkeys                   901234567890123456789012345678901234567890123456789012345678
Colobus monkey                      KSLWDQGCFSMIIKNLKIEDSDTYICEVEDKKEEVELLVFGLTASSDTHLLQGQSLTLTL
Colobus guereza                     KSLWDQGCFSMIIKNLKIEDSDTYICEVEDKKEEVELLVFGLTASSDTHLLQGQSLTLTL
Angolan colobus                     KSLWDQGCFSMIIKNLKIEDSDTYICEVEDKKEEVELLVFGLTASSDTHLLQGQSLTLTL
African green monkey                KSLWDQGCFSMIIKNLKIEDSETYICEVENKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Vervet monkey                       KSLWDQGCFSMIIKNLKIEDSETYICEVENKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Sabaeus monkey                      KSLWDQGCFSMIIKNLKIEDSETYICEVENKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Tantalus monkey                     KSLWDQGCFSMIIKNLKIEDSETYICEVENKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Red guenon                          KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Sooty mangabey                      KSLWDQGCFSMIIKNLKIEDSETYICEVENKKEEVELLVFGLTANSDTHLLEGQSLTLTL
Mandrill                            KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLEGQSLTLTL
Black snub-nose monkey              KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Golden snub-nose                    KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Leaf monkey                         KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVKLLVFGLTANSDTHLLQGQSLTLTL
Francoi's langur                    KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVKLLVFGLTANSDTHLLQGQSLTLTL
Pig-tailed macaque                  KSLWDQGCFSMIIKNLKIEDSNTYICEVENEKEEVELLVFGLTANSDTHLLEGQSLTLTL
Rhesus macaque                      KSLWDQGCFSMIIKNLKIEDSDTYICEVENKKEEVELLVFGLTANSDTHLLEGQSLTLTL
Cynomolgus macaque                  KSLWDQGCFSMIIKNLKIEDSDTYICEVENKKEEVELLVFGLTANSDTHLLEGQSLTLTL
Japanese macaque                    KSLWDQGCFSMIIKNLKIEDSDTYICEVENKKEEVELLVFGLTANSDTHLLEGQSLTLTL
Wolf's guenon                       KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Talapoin                            KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLQGQSLTLTL
Gray-cheeked mangabey               KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLEGQSLTLTL
Olive baboon                        KSLWDQGCFSMIIKNLKIEDSETYICEVEDKKEEVELLVFGLTANSDTHLLEGQSLTLTL

                                    60s       70s       80s       90s       100s      110s
New World Monkeys                   901234567890123456789012345678901234567890123456789012345678
Coppery titi                        KSSWDRGSFPLIIKNVQVEDSETYICEVESKKEEVELQVFGLTATPDTHLLQGQNLTLTL
Marmoset                            QSSWDRGSFPLIIRNVQVEDSETYICEVESKKEEVELQVFGLTVNPDTHLLQGQSLTLTL
Squirrel monkey                     RSSWDRGSFPLLIKDARIEDSETYICEVESKKEEVELQVFGLTANPDTHLLQGQSLTLTL
Bolivian squirrel monkey            KSSWDRGSFPLLIKDARIEDSETYICEVESKKEEVELQVFGLTANPDTHLLQGQSLTLTL
Howler monkey                       KSSWDRGSFPLIIKNVQVEDSETYICEVESKKEEVELQVFGLTANPDTHLLQGQSLTLTL
Bolivian red howler monkey          KSSWDRGSFPLIIKNVQVEDSETYICEVESKKEEVELQVFGLTANPDTHLLQGQSLTLTL
Panamanian white-throated capuchin  KSSWDRGSFPLLIKNVRVEDSETYICEVEGKKEEVELQVFGLTANPDTHLLQGQSLTLTL
Nancy Ma's owl monkey               KSSWDRGSFPLIIKNVQVEDSETYICEVERKKEEVELQVFGLTASPDTNLLQGQSLTLTL
Azara's owl monkey                  KSSWDRGSFPLIIKNVQVEDSETYICEVERKKEEVELQVFGLTASPDTHLLQGQSLTLTL
Spix's owl monkey                   KSSWDRGSFPLIIKNVQVEDSETYICEVERKKEEVELQVFGLTASPDTHLLQGQSLTLTL

                                    60s       70s       80s       90s       100s      110s
Prosimians                          901234567890123456789012345678901234567890123456789012345678
Tarsier                             KSLWDQGSFPLIIRNLEVGDSGTYICEVQDRKTEVELLVFALTANSNTRLLQGQSLTLSL
Sunda flying lemur                  KNLWDQGSFPLVIKNLEVEDSGMYICEVENRKIEVELLVFGLIANSDTRLLQGQSLTLTL
Gray mouse lemur                    KNLWDQGSFPLVIKNLEMKDSGSYICEVEDKK-EVELLVFGLTANSGTRVLHGQSLTLTL
Coquerel's sifaka                   KNLWDQGSFPLIIKNLEMQDSGTYICEVEDKK-EVELLVFGLTANSGTRVLHGQSLTLTL
```

C.

```
                                    120s       130s       140s       150s       160s       170s
Apes                                901234567890123456789012345678901234567890123456789012345678
Human                               ESPPGSSPSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIVVLA
Chimp                               ESPPGSSPSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIVVLA
Bonobo                              ESPPGSSPSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIVVLA
Gorilla                             ESPPGSSPSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQEKVEFKIDIVVLA
Bornean orangutan                   ESPPGSSPSVQCRSPTGKNIQAGKTLSVSQLELQDSGTRTCAVLQDQKKVEFKIDIVVLA
White-cheeked gibbon                EGPPGSSPSVQCRSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQDQKKVEFKIDIVVLA
Agile gibbon                        ESPPGSSPSVQCRSPRGKNIQGGKTLSVPQLELQDSGTWTCTVLQDQKKVEFKIDIVVLA
Siamang                             EGPPGSSPSVQCRSPRGKNIQGGKTLSVPQLELQDSGTWTCTVLQDQKKVEFKIDIVVLA

                                    120s       130s       140s       150s       160s       170s
Old World Monkeys                   901234567890123456789012345678901234567890123456789012345678
Colobus monkey                      ESPPGTSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGTWTCTVSQDQKRVEFKIDIVVLA
Colobus guereza                     ESPPGTSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGTWTCTVSQDQKRVEFKIDIVVLA
Angolan colobus                     ESPPGTSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGTWTCTISQDQKRVEFKIDIVVLA
African green monkey                ESPPGSSPSVKCRSPRGKNIQVGRTLSVPQLERQDSGTWTCTVSQDQNTVEFKIDIVVLA
Vervet monkey                       ESPPGSSPSVKCRSPRGKNIQVGRTLSVPQLERQDSGTWTCTVSQDQNTVEFKIDIVVLA
Sabaeus monkey                      ESPPGSSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQNTVEFKIDIVVLA
Tantalus monkey                     ESPPGSSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQNTVEFKIDIVVLA
Red guenon                          ESPPGSSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQNTVEFKIDIVVLA
Sooty mangabey                      ESPPGSSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Mandrill                            ESPPGSSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Black snub-nose monkey              ESPPGSSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGIWTCTVSQDQKTVEFKIDIMVLA
Golden snub-nose                    ESPPGSSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGIWTCTVSQDQKTVEFKIDIMVLA
Leaf monkey                         ESPPGSSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGIWTCTVSQDQKTVEFKIDIVVLA
Francoi's langur                    ESPPGSSPSVQCRSPRGKNIQGGKTLSVPQLERQDSGIWTCTVSQDQKTVEFKIDIVVLA
Pig-tailed macaque                  ESPPGSSPSVKCRSPGGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Rhesus macaque                      ESPPGSSPSVKCRSPGGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Cynomolgus macaque                  ESPPGSSPSVKCRSPGGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Japanese macaque                    ESPPGSSPSVKCRSPGGKNIQGGRTISVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Wolf's guenon                       ESPPGSSPSVKCRSPRGKNIQRGRTLSVPQLERQDSGTWTCTVSQDQKTVEFNIDIVVLA
Talapoin                            ESPPGSSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCTVSQDQKTVEFKIDIVVLA
Gray-cheeked mangabey               ESPPGTSPSVKCRSPRGKNIQVGRTLSVPQLERQDSGTWTCNVSQDQKTVEFKIDIVVLA
Olive baboon                        ESPPGTSPSVKCRSPRGKNIQGGRTLSVPQLERQDSGTWTCNVSQDQKTVEFKIDIVVLA

                                    120s       130s       140s       150s       160s       170s
New World Monkeys                   901234567890123456789012345678901234567890123456789012345678
Coppery titi                        ESPPGSSPSVECTSPRGKRISGMKTLFLSQLVIQDSGTGKCALCQHRELV-FQINIVVLA
Marmoset                            ESPPGSSPSVECMSPRGKTIRGMKTLFMSQLEIQDSGTWKCTVSQHLELV-FKINIVVLA
Squirrel monkey                     ESPPGSSPSVECTSPRGKRIRGRKTLSVSQLGIPDSGTWKCTVFQHLELV-FEINIVVLA
Bolivian squirrel monkey            ESPPGSSPSVECTSPRGKRIRGRKTLSVSQLGIPDSGTWKCTVFQHLELV-FEINIVVLA
Howler monkey                       ESPPGSSPSVECTSPRGKRIQGMKSLSLSQLEIQDSGTWKCTVSQHPQLV-FKINIVVLA
Bolivian red howler monkey          ESPPGSSPSVECTSPRGKRIQGMKSLSLSQLEIQDSGTWKCTVSQHPQLV-FKINIVVLA
Panamanian white-throated capuchin  ESPPGSSPSVECTSPRGKRIQGMKTLSLSQLEIQDSGTWKCTVSQHLELV-FEINIVVLA
Nancy Ma's owl monkey               ESPPGSSPSVECTSPRGKRIQGMKNLSVSQLEIQDSGTWKCTVSQRPELL-FKINVVVLA
Azara's owl monkey                  ESPPGSSPSVECTSPRGKRIQGMKTLSVSQLEIQDSGTWKCTVSQHPELL-FKINVVVLA
Spix's owl monkey                   ESPPGSSPSVECTSPRGKRIQGMKTLSVSQLEIQDSGTWKCTVSQHPELL-FKINVVVLA

                                    120s       130s       140s       150s       160s       170s
Prosimians                          901234567890123456789012345678901234567890123456789012345678
Tarsier                             EGPQGRNPSLQCQGPGNKRISGVGSLSLSQLGPQHSGRWTCAVSQDQKTLEFSKDVVVLV
Sunda flying lemur                  ESPPDSNPSVQWKSPGNKHTNGVKTLSVSQLGSQESGTWTCTVSKDQKTLALNINILVLA
Gray mouse lemur                    ESPRGSSPSVHCKSPGNKNINGVSLLSLPQLGIQDSGTWTCTVSQDRQTLAFKIHISVLA
Coquerel's sifaka                   ESPRGSSPSVQCKSPRNKNINGVSVLSVSQLGLQDSGTWTCTVSQDRHTLAFKIHISVLA
```

FIGURE 5

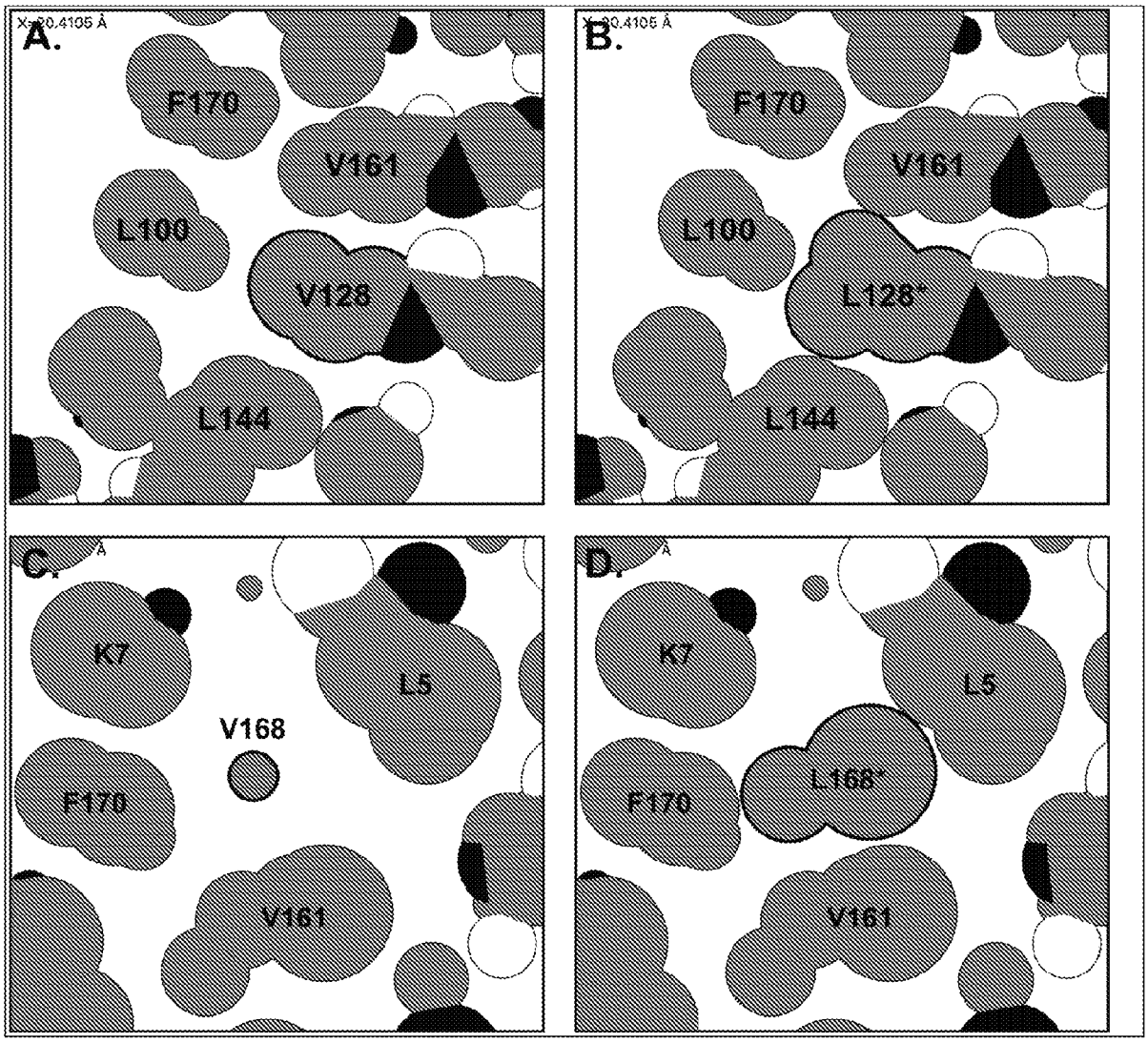

A.
F170
V161
L100
V128
L144
B.
F170
V161
L100
L128*
L144
C.
K7
L5
V168
F170
V161
D.
K7
L5
L168*
F170
V161

FIGURE 6

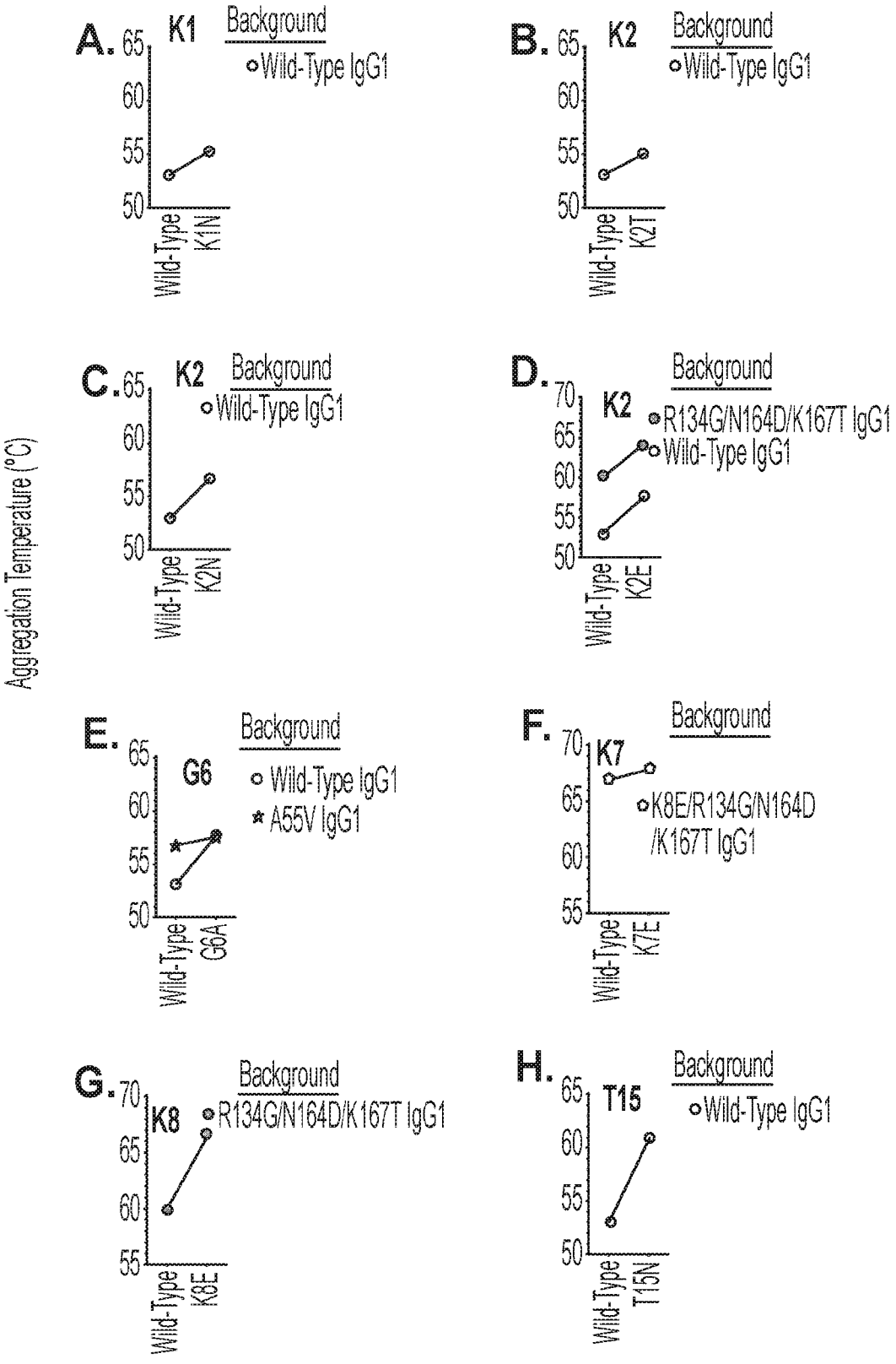

A.
K1
Background
Wild-Type IgG1
65
60
55
50
Wild-Type
K1N
B.
K2
Background
Wild-Type IgG1
65
60
55
50
Wild-Type
K2T
C.
K2
Background
Wild-Type IgG1
65
60
55
50
Wild-Type
K2N
D.
Background
K2
R134G/N164D/K167T IgG1
Wild-Type IgG1
70
65
60
55
50
Wild-Type
K2E
E.
Background
G6
Wild-Type IgG1
A55V IgG1
65
60
55
50
Wild-Type
G6A
F.
Background
K7
K8E/R134G/N164D
/K167T IgG1
70
65
60
55
Wild-Type
K7E
G.
Background
K8
R134G/N164D/K167T IgG1
70
65
60
55
Wild-Type
K8E
H.
Background
T15
Wild-Type IgG1
65
60
55
50
Wild-Type
T15N
Aggregation Temperature (°C)

FIGURE 6, continued

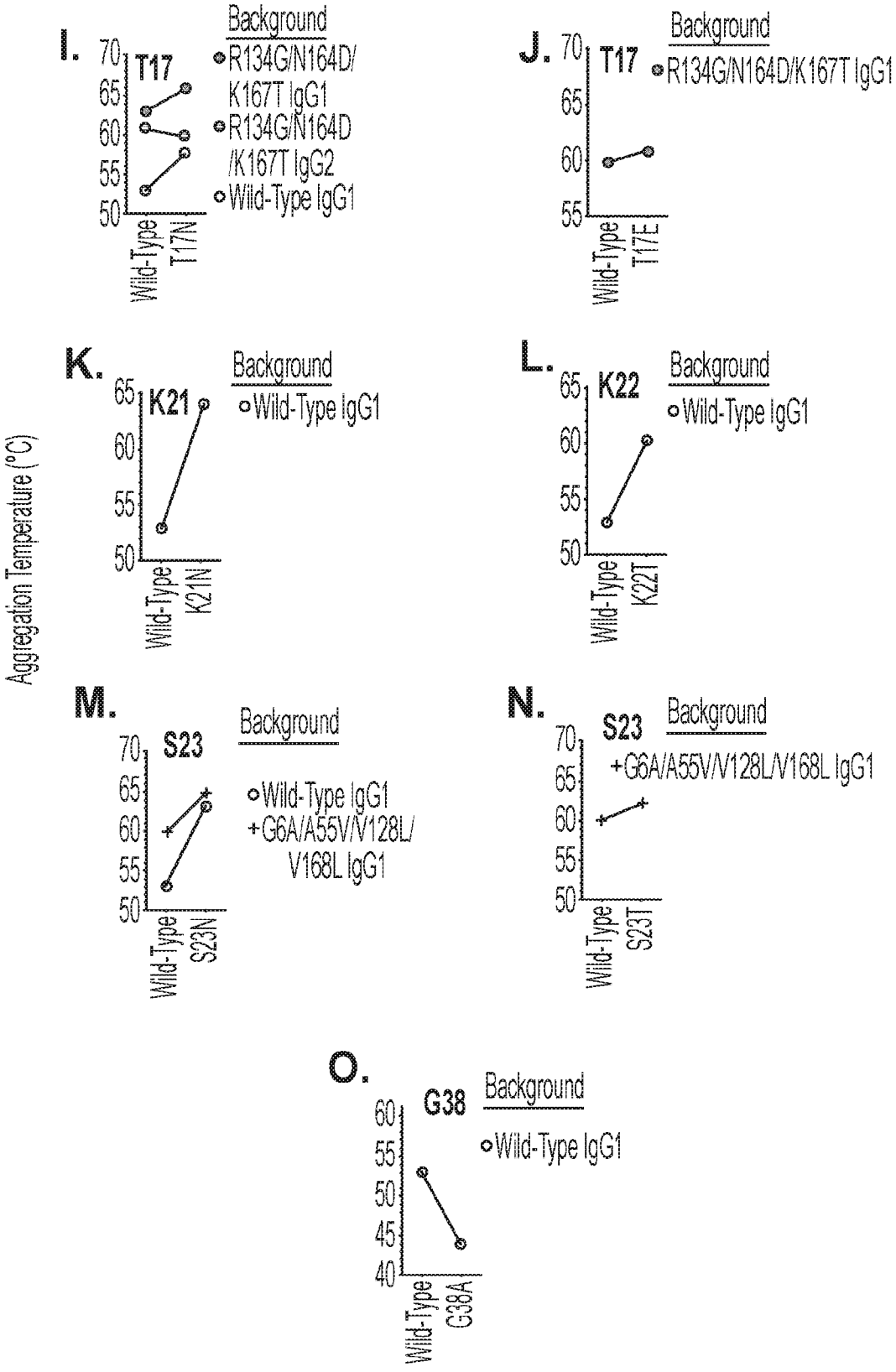


FIGURE 6, continued

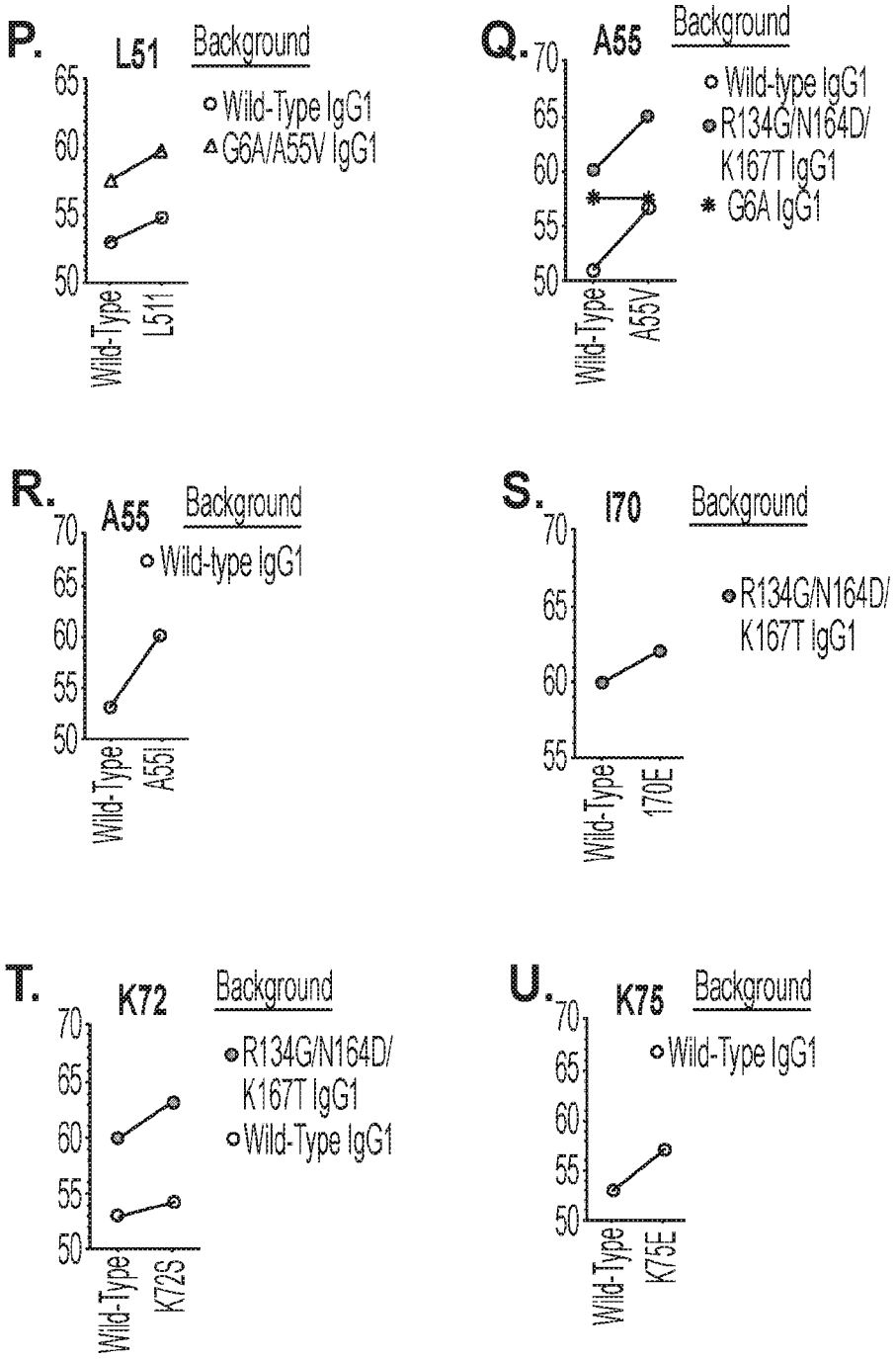


FIGURE 6, continued

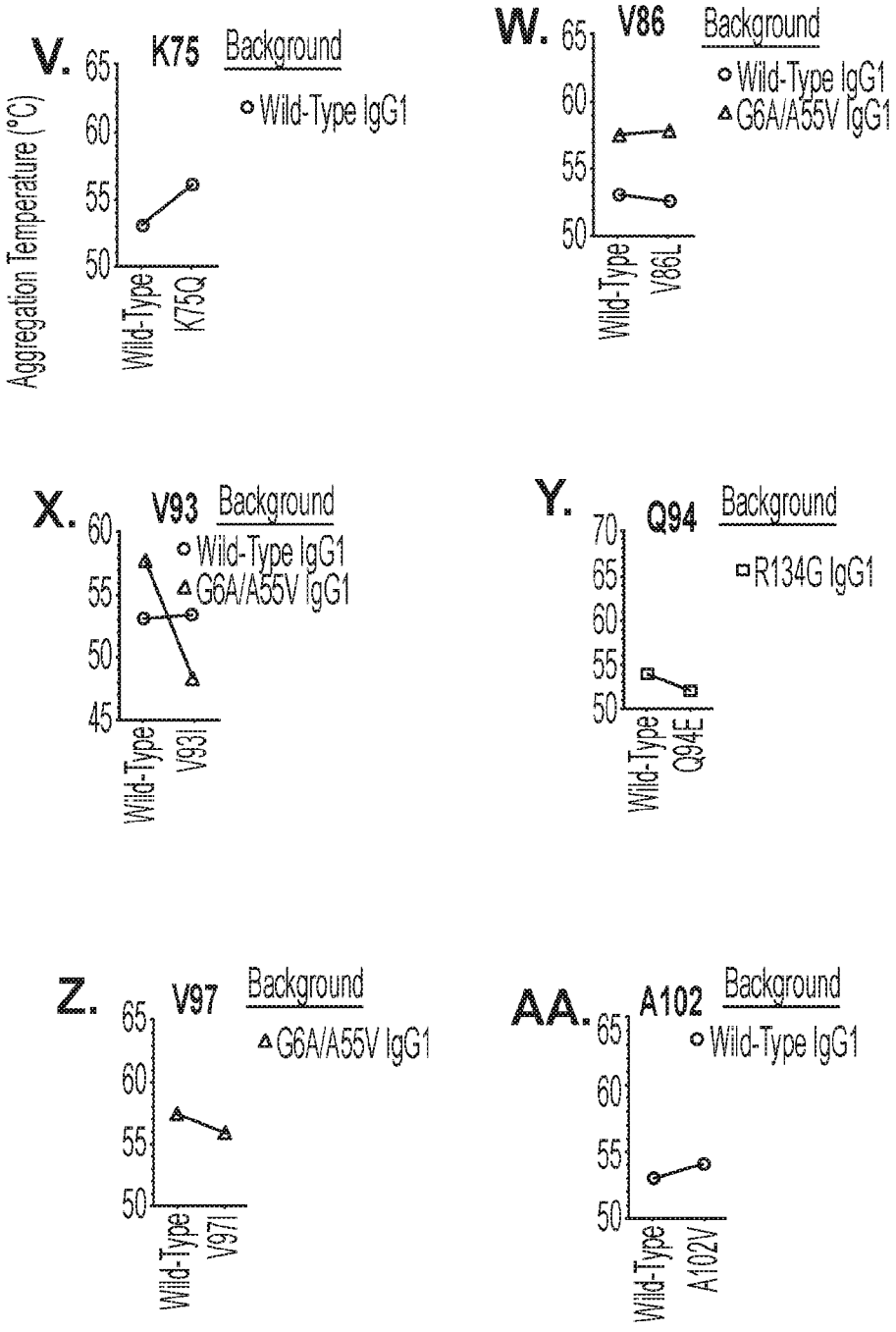


FIGURE 6, continued

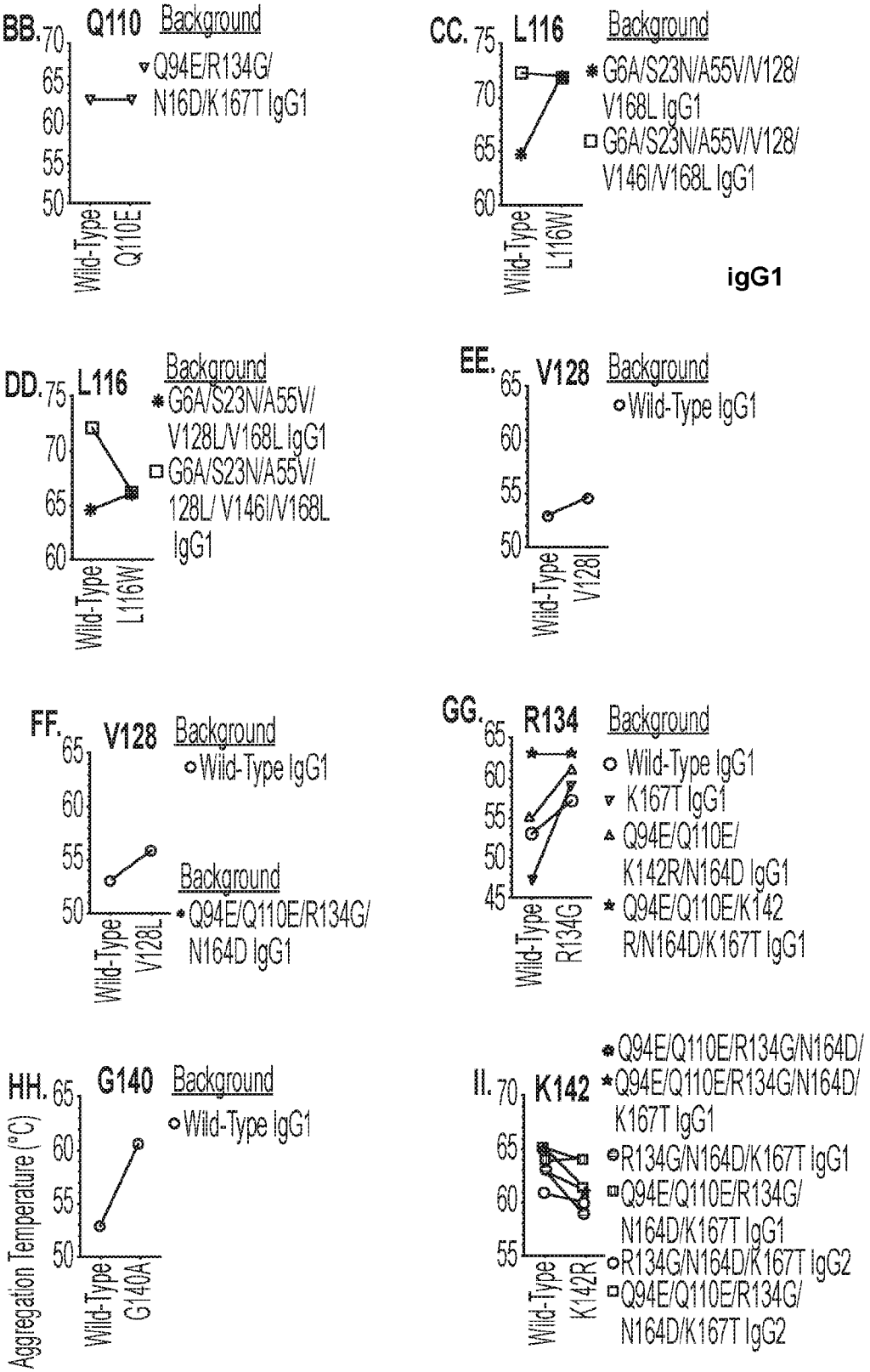


FIGURE 6, continued

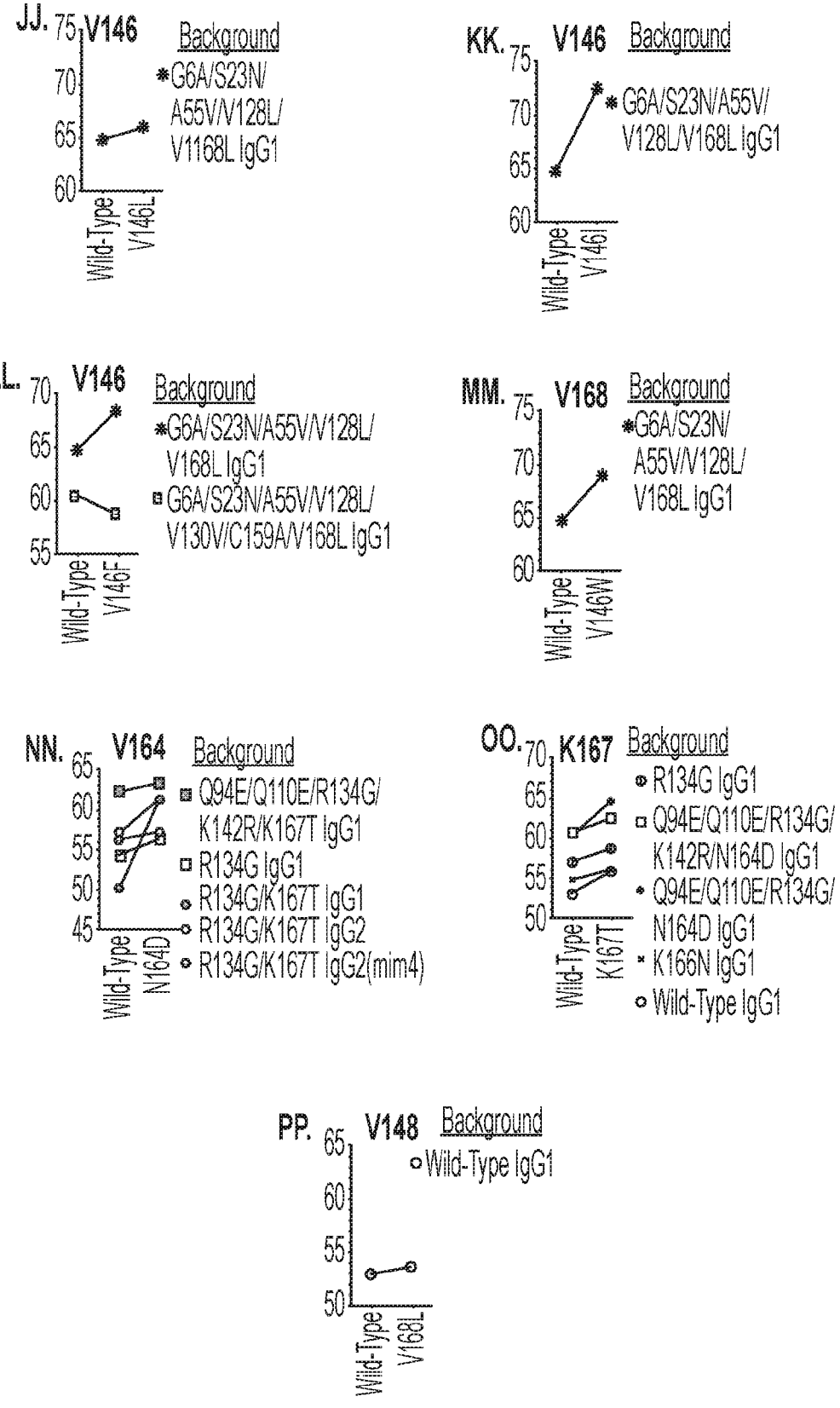


FIGURE 6, continued 14/41

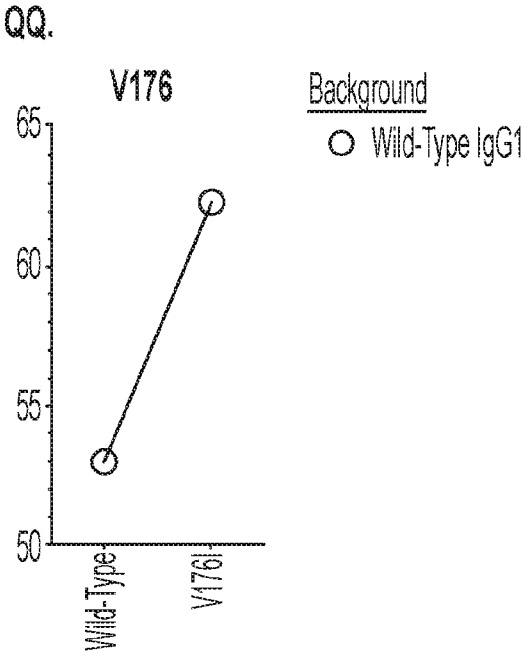


FIGURE 7

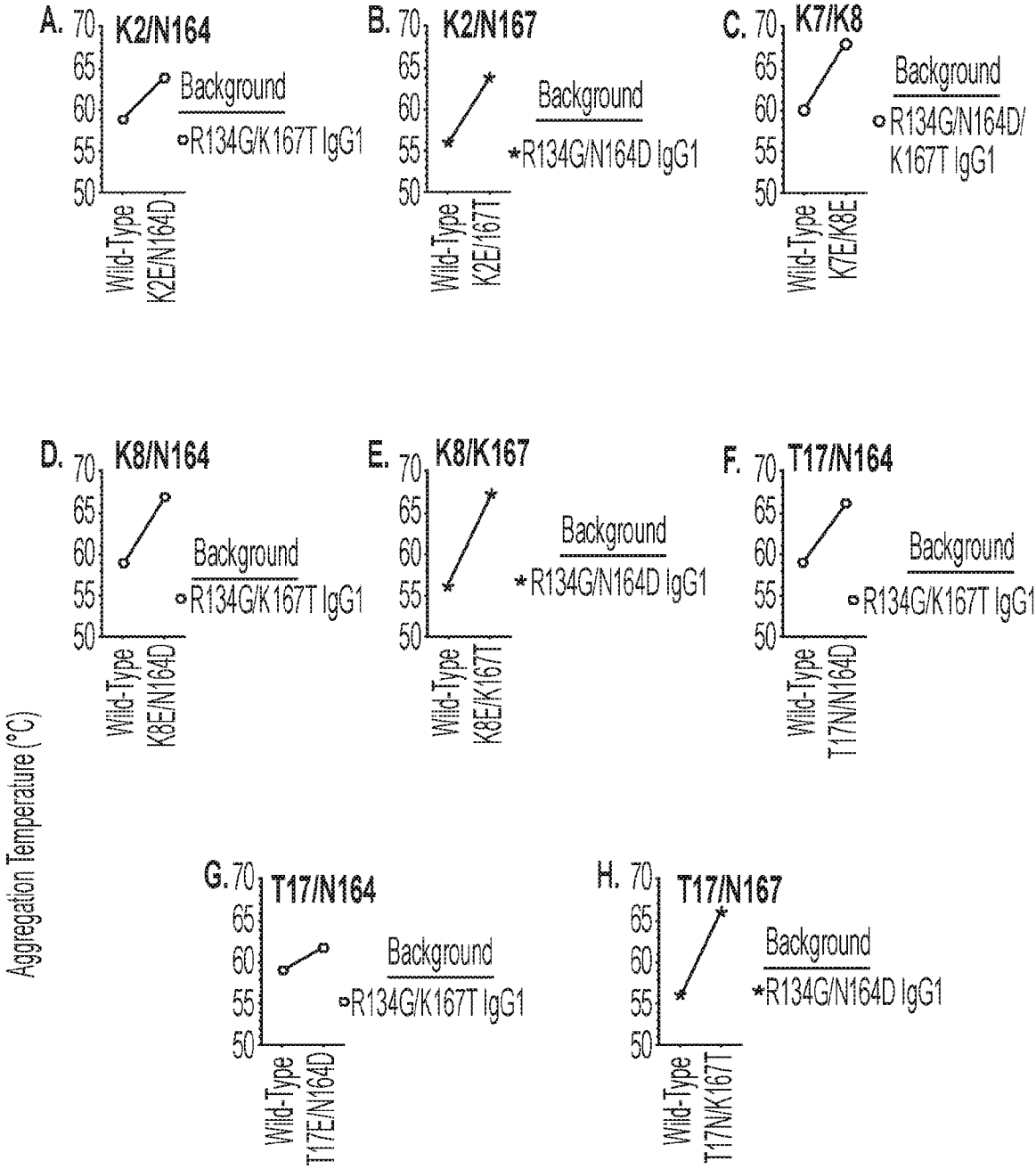

A.
K2/N164
Background
R134G/K167T IgG1
Wild-Type
K2E/N164D
B.
K2/N167
Background
*R134G/N164D IgG1
Wild-Type
K2E/167T
C.
K7/K8
Background
R134G/N164D/
K167T IgG1
Wild-Type
K7E/K8E
D.
K8/N164
Background
R134G/K167T IgG1
Wild-Type
K8E/N164D
E.
K8/K167
Background
*R134G/N164D IgG1
Wild-Type
K8E/K167T
F.
T17/N164
Background
R134G/K167T IgG1
Wild-Type
T17N/N164D
G.
T17/N164
Background
R134G/K167T IgG1
Wild-Type
T17E/N164D
H.
T17/N167
Background
*R134G/N164D IgG1
Wild-Type
T17N/K167T
70
65
60
55
50
Aggregation Temperature (°C)

FIGURE 7, continued

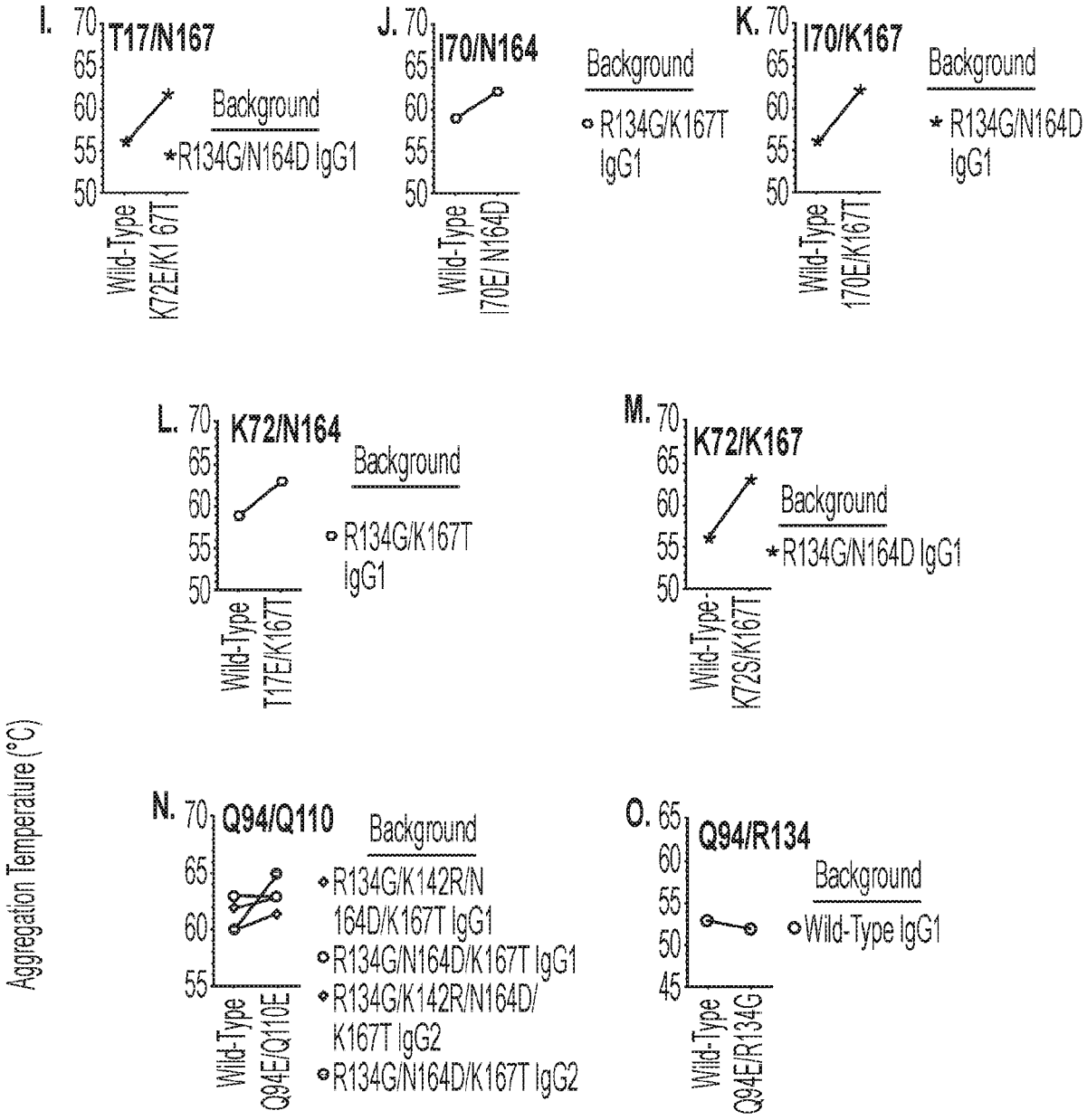


FIGURE 7, continued

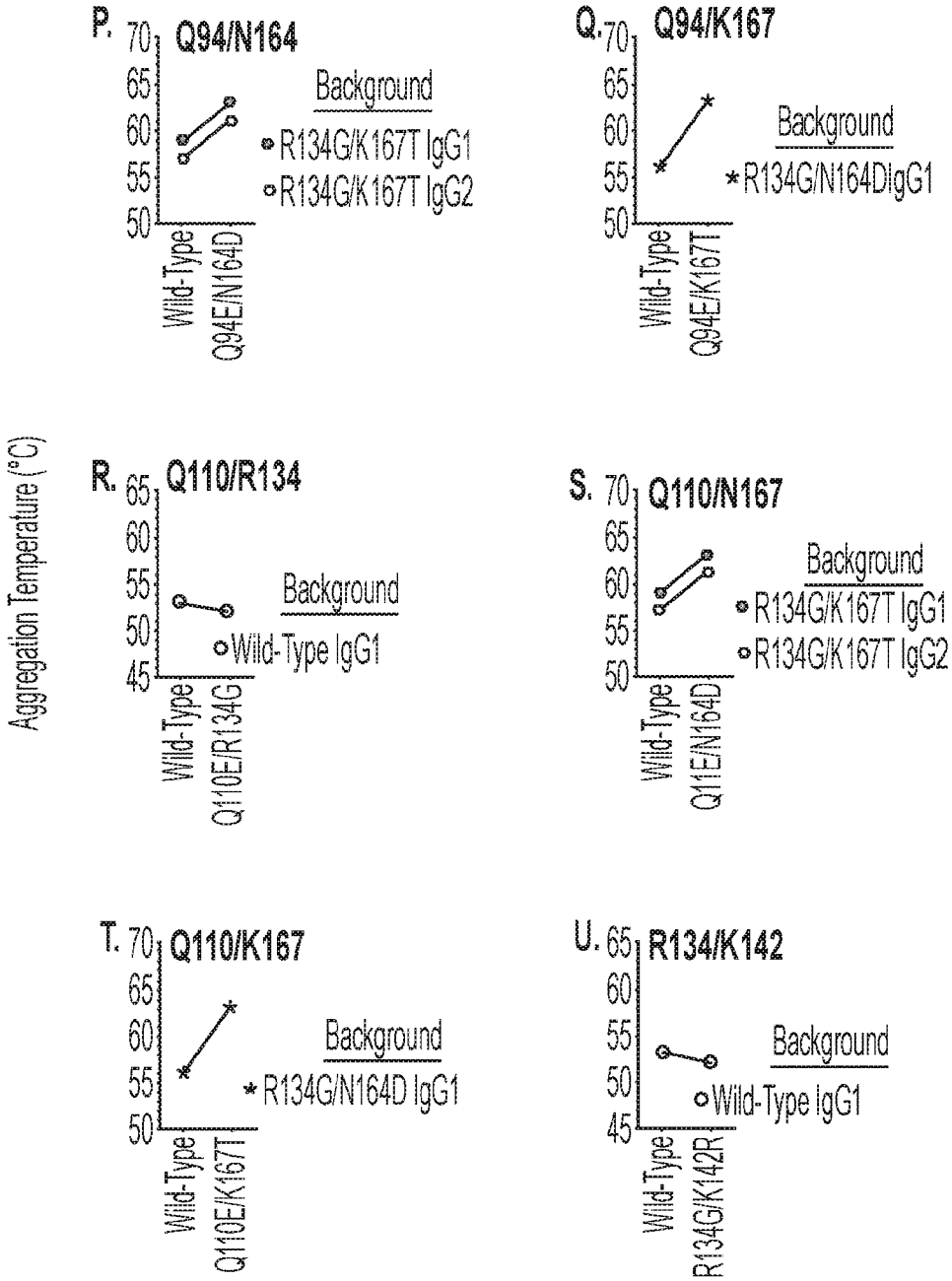


FIGURE 7, continued

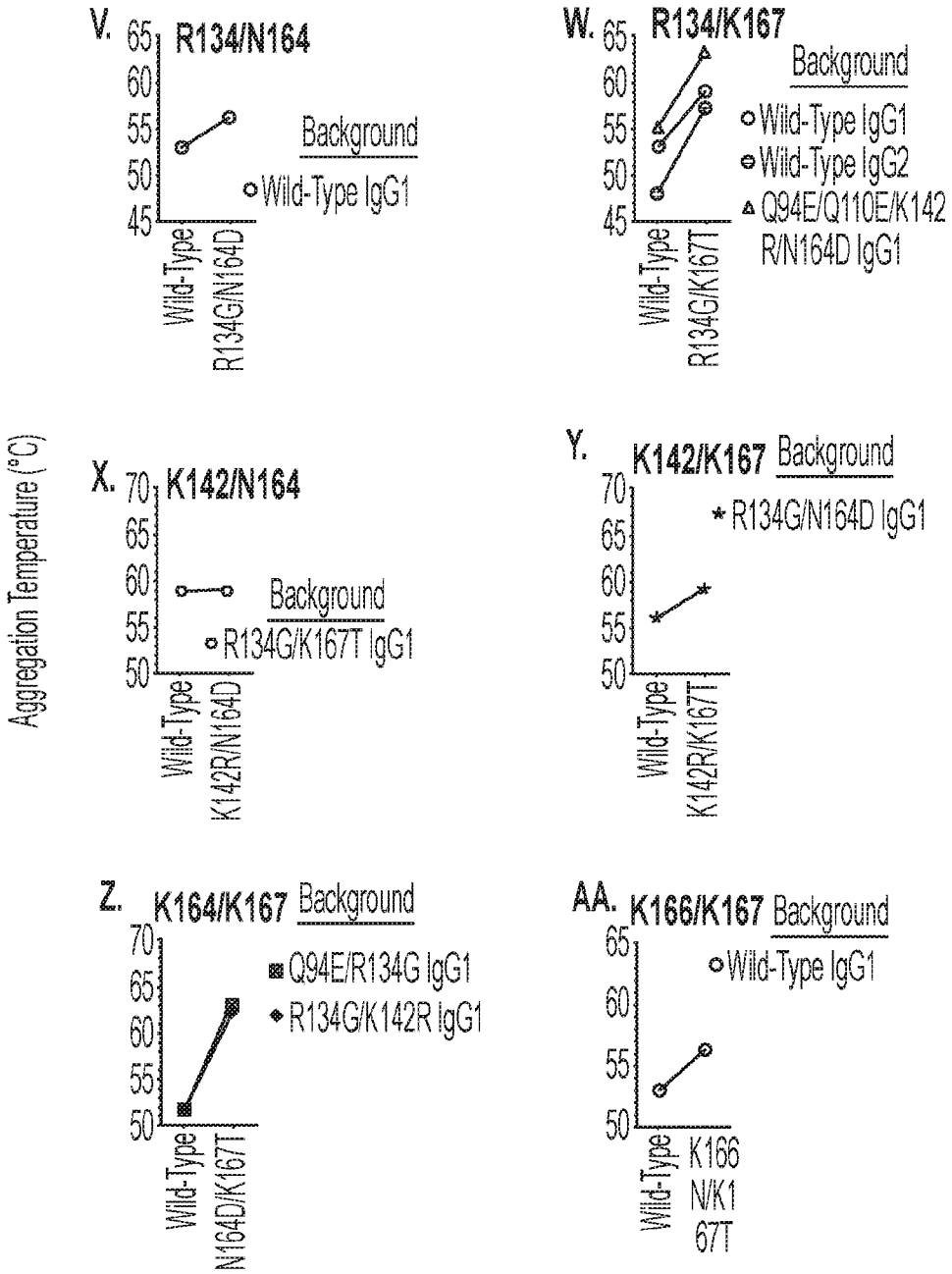


FIGURE 8

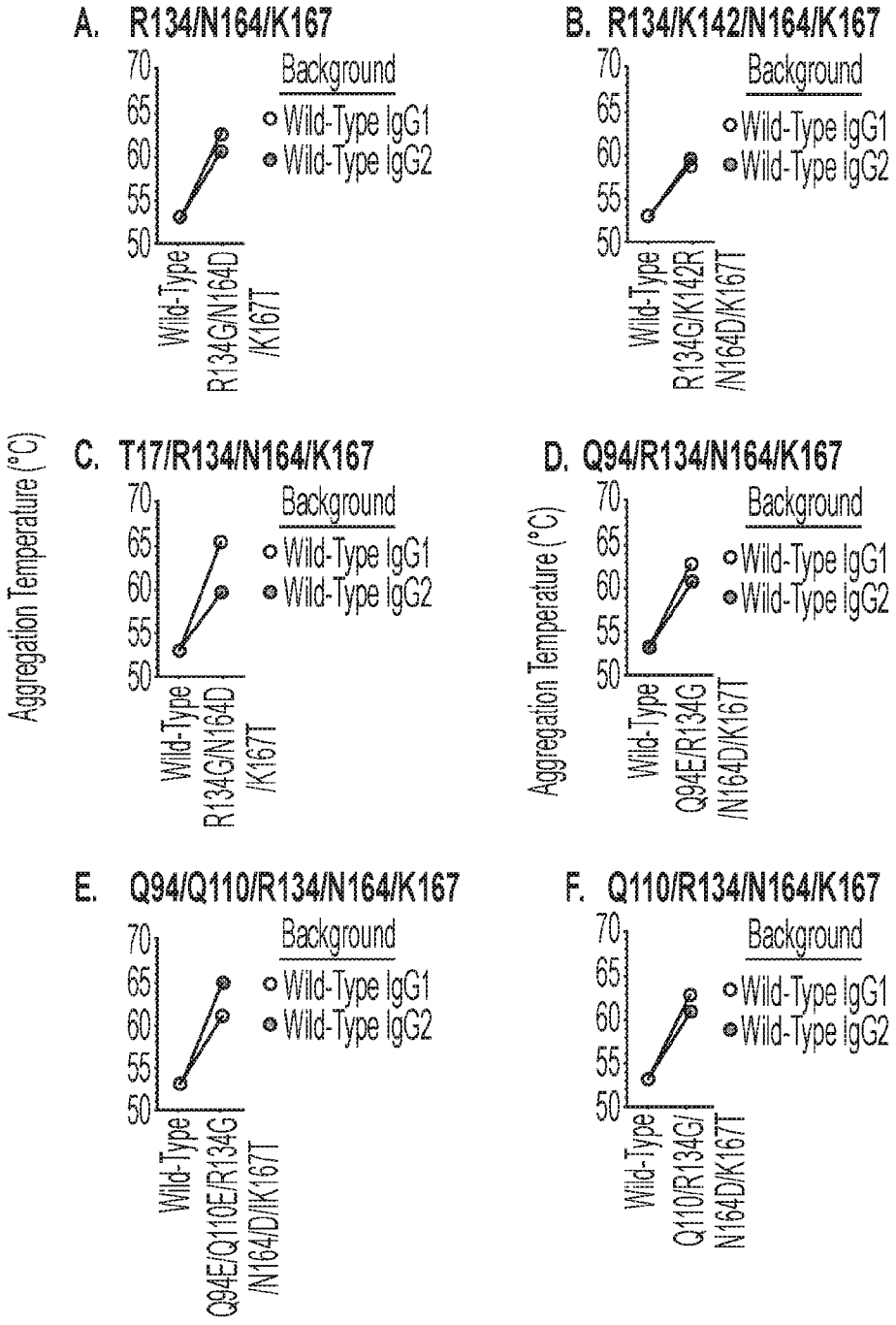
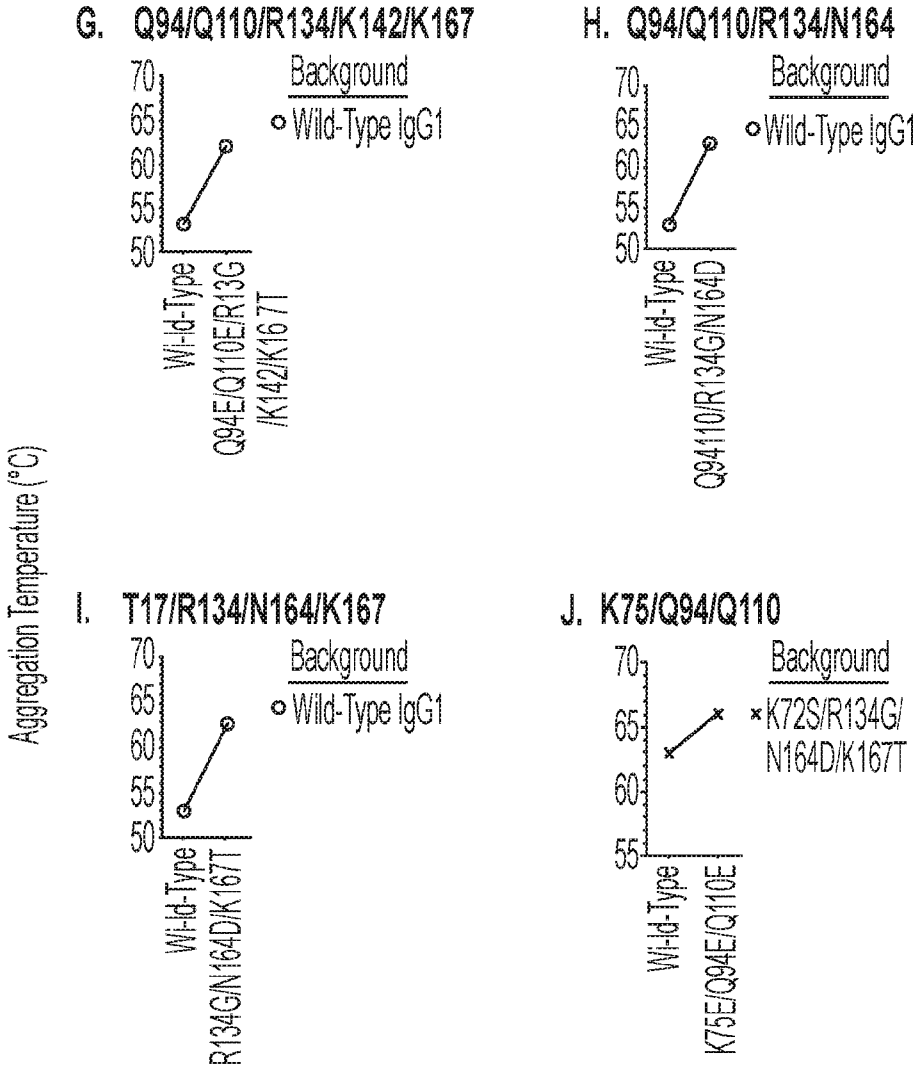

A. R134/N164/K167
B. R134/K142/N164/K167
C. T17/R134/N164/K167
D. Q94/R134/N164/K167
E. Q94/Q110/R134/N164/K167
F. Q110/R134/N164/K167
Aggregation Temperature (°C)
70
65
60
55
50
Background
Wild-Type IgG1
Wild-Type IgG2
Wild-Type
R134G/N164D /K167T
R134G/K142R /N164D/K167T
Q94E/R134G /N164D/K167T
Q94E/Q110E/R134G /N164D/K167T
Q110/R134G/ N164D/K167T

FIGURE 8, continued



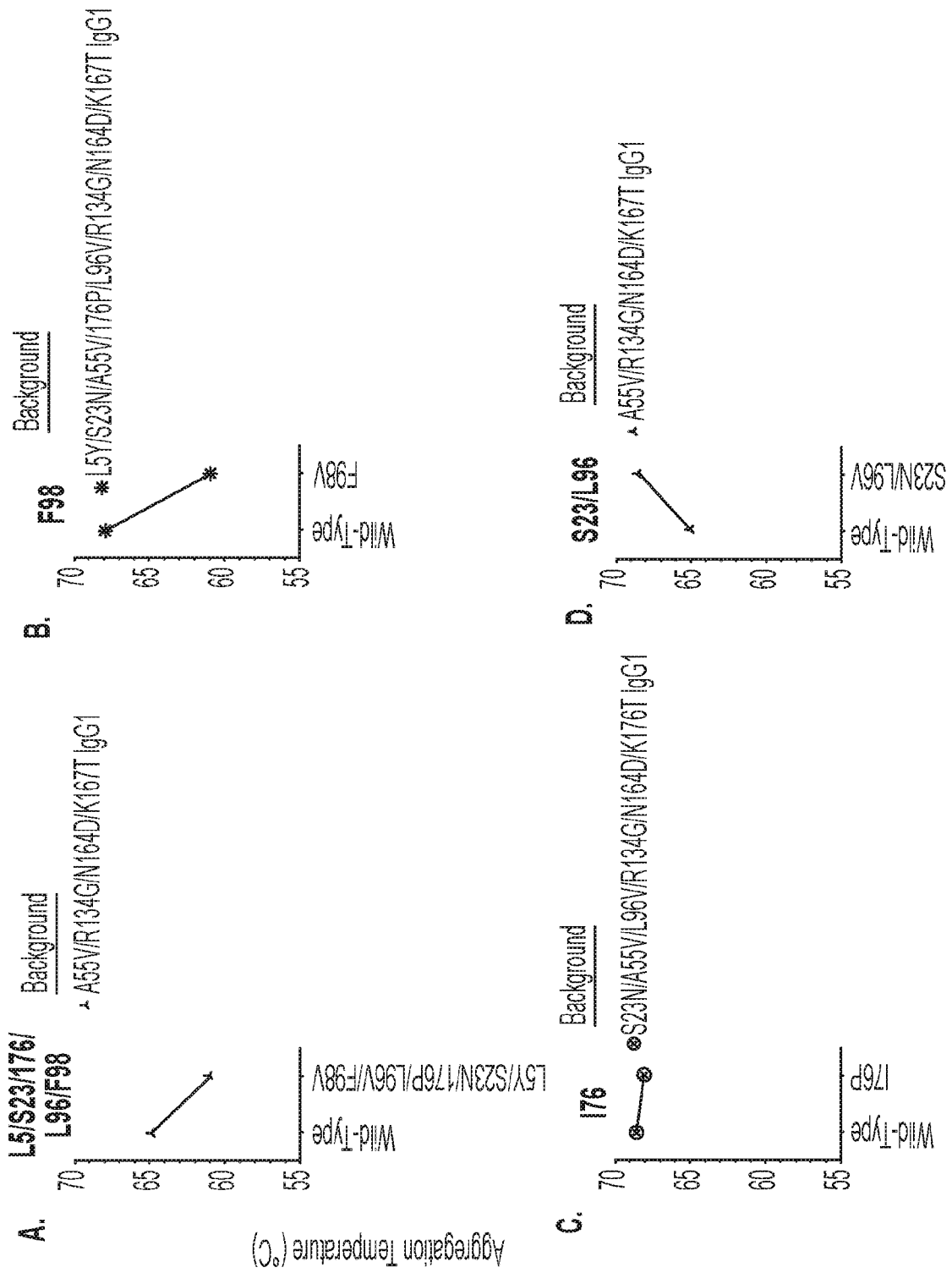
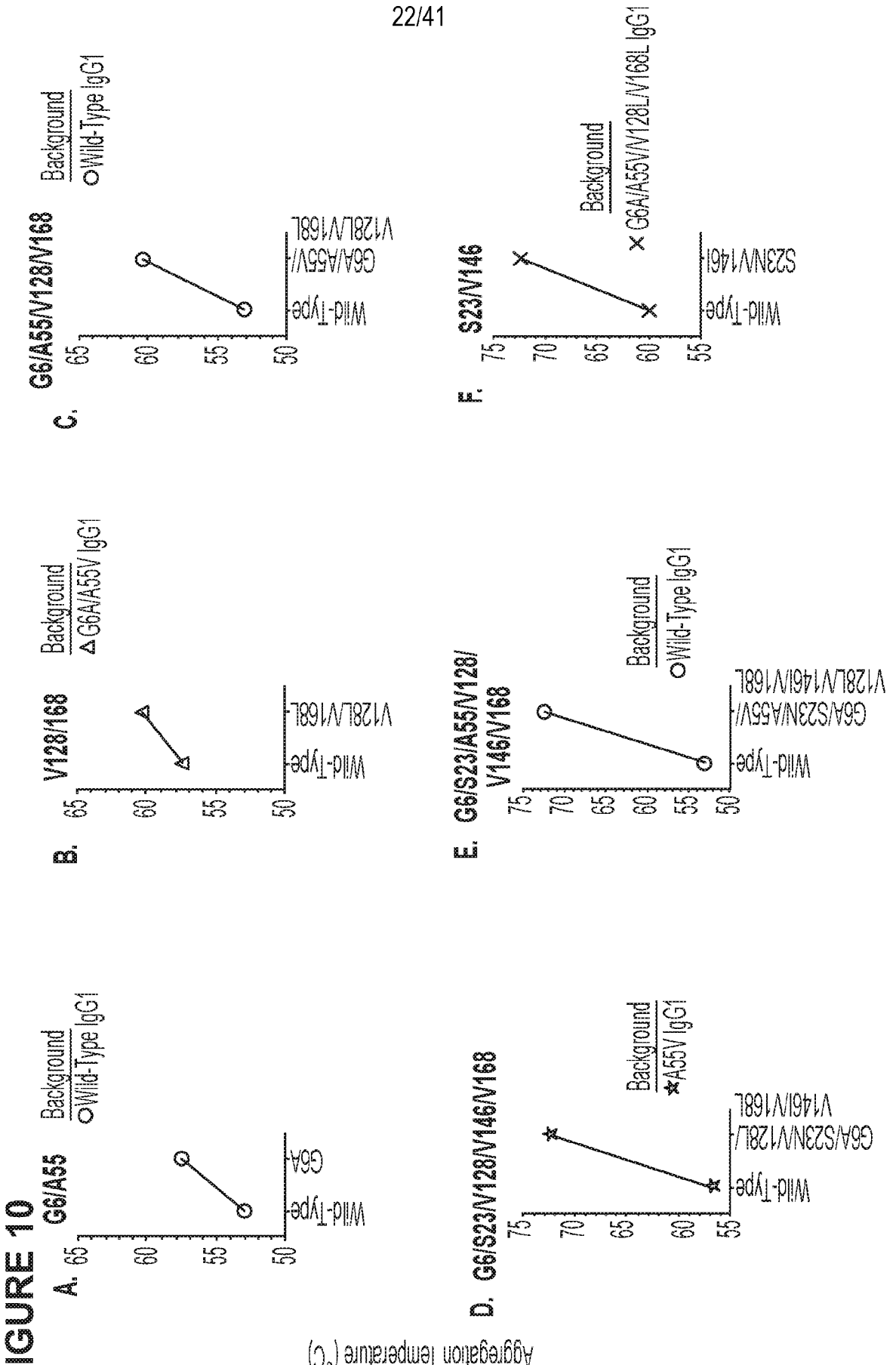

A.
L5/S23/176/L96/F98
Background
A55V/R134G/N164D/K167T IgG1
Wild-Type
L5Y/S23N/176P/L96V/F98V
70
65
60
55
Aggregation Temperature (°C)
B.
F98
Background
L5Y/S23N/A55V/I76P/L96V/R134G/N164D/K167T IgG1
Wild-Type
F98V
C.
I76
Background
S23N/A55V/L96V/R134G/N164D/K176T IgG1
Wild-Type
I76P
D.
S23/L96
Background
A55V/R134G/N164D/K167T IgG1
Wild-Type
S23N/L96V

FIGURE 9

FIGURE 10


A.
G6/A55
Background
Wild-Type IgG1
Wild-Type
G6A
B.
V128/168
Background
G6A/A55V IgG1
Wild-Type
V128L/V168L
C.
G6/A55/V128/V168
Background
Wild-Type IgG1
Wild-Type
G6A/A55V/V128L/V168L
D.
G6/S23/V128/V146/V168
Background
A55V IgG1
Wild-Type
G6A/S23N/V128L/V146I/V168L
E.
G6/S23/A55/V128/V146/V168
Background
Wild-Type IgG1
Wild-Type
G6A/S23N/A55V/V128L/V146I/V168L
F.
S23/V146
Background
G6A/A55V/V128L/V168L IgG1
Wild-Type
S23N/V146I
65
60
55
50
75
70
65
60
55
Aggregation Temperature (°C)

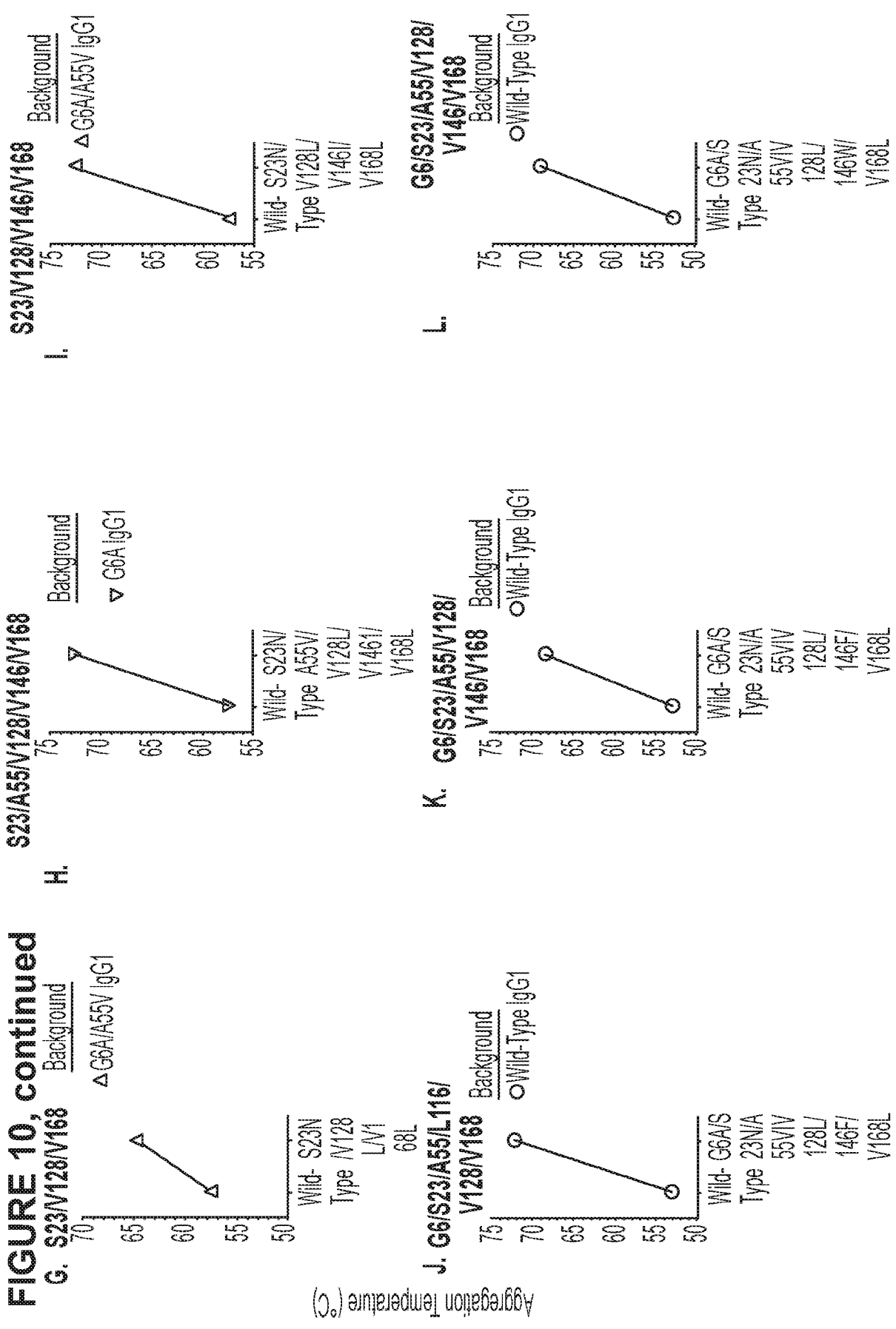
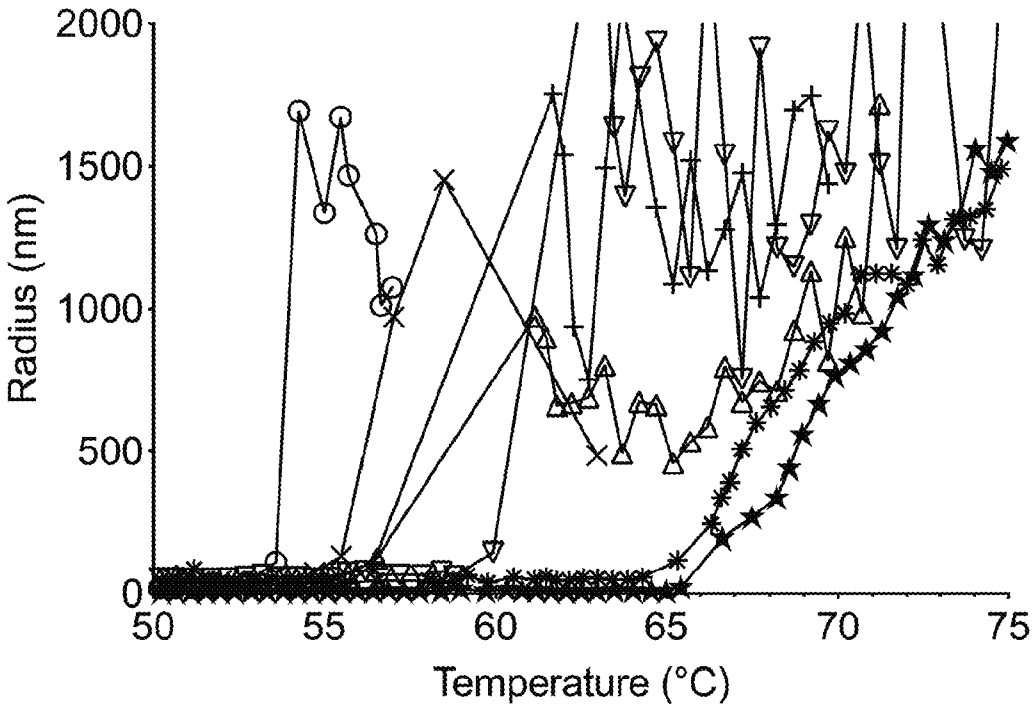


FIGURE 10, continued
G. S23/V128/V168
Background
△G6A/A55V IgG1
Wild- S23N
Type /V128
L/V1
68L
H. S23/A55/V128/V146/V168
Background
▽G6A IgG1
Wild- S23N/
Type A55V/
V128L/
V1461/
V168L
I. S23/V128/V146/V168
Background
△G6A/A55V IgG1
Wild- S23N/
Type V128L/
V146I/
V168L
J. G6/S23/A55/L116/
V128/V168
Background
○Wild-Type IgG1
Wild- G6A/S
Type 23N/A
55V/V
128L/
146F/
V168L
K. G6/S23/A55/V128/
V146/V168
Background
○Wild-Type IgG1
Wild- G6A/S
Type 23N/A
55V/V
128L/
146F/
V168L
L.
G6/S23/A55/V128/
V146/V168
Background
○Wild-Type IgG1
Wild- G6A/S
Type 23N/A
55V/V
128L/
146W/
V168L
Aggregation Temperature (°C)
75
70
65
60
55
50

FIGURE 11



○ Wild-Type IgG1
\+ G6A IgG1
× A55V IgG1
△ G6A/A55V IgG1
▽ G6A/A55V/V128L/V168L IgG1
✳ G6A/S23N/A55V/V128L/V168L IgG1
★ G6A/S23N/A55V/V128L/V146I/V168L IgG1

FIGURE 12

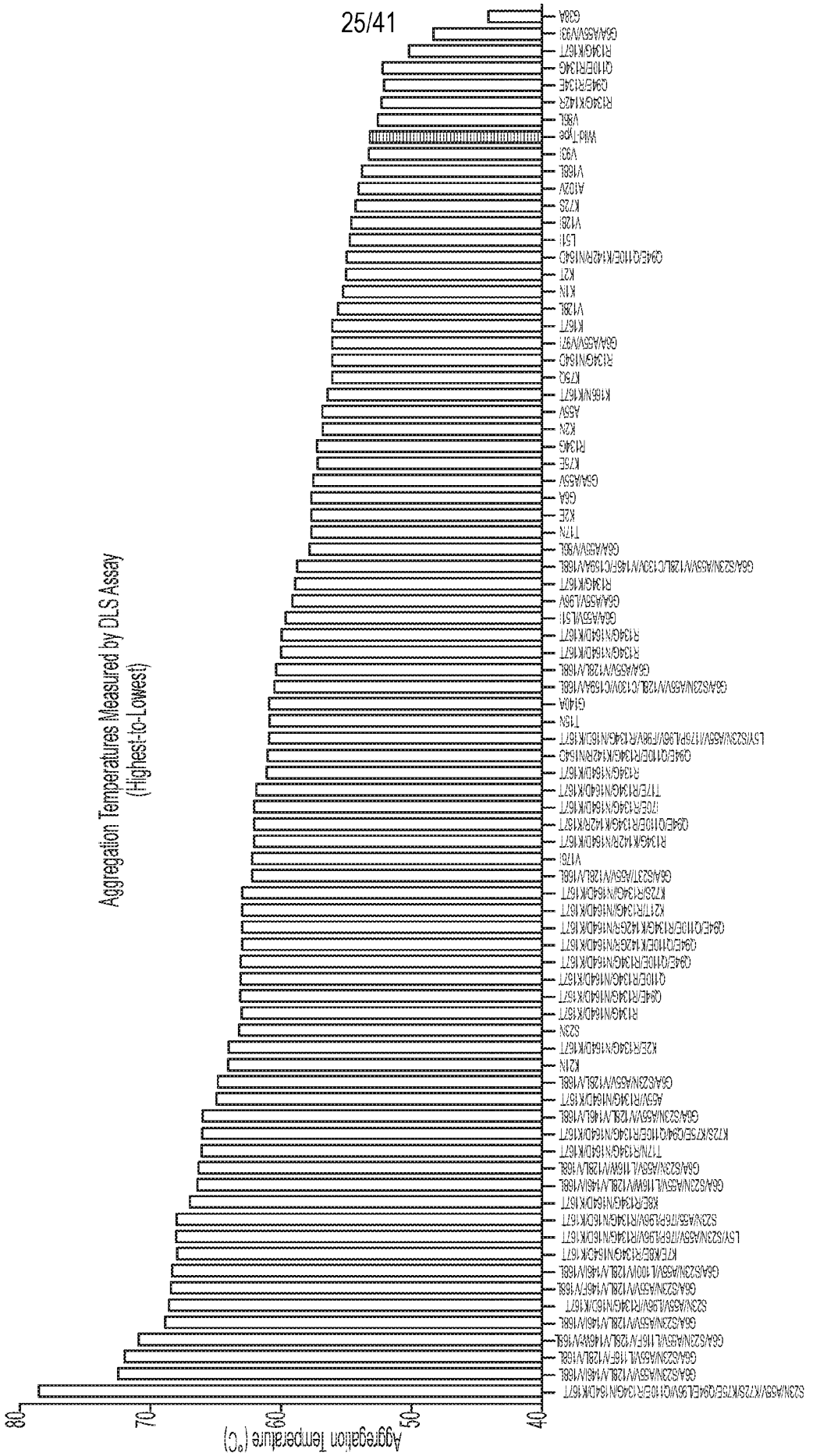

Aggregation Temperatures Measured by DLS Assay
(Highest-to-Lowest)
Aggregation Temperature (°C)
80
70
60
50
40
S23N/A55V/K72S/K72S/Q94E/L95V/Q110E/R134G/N164D/K167T
G6A/S23N/A55V/V128L/V146I/V168L
G6A/S23N/A55V/L116F/V128L/V168L
G6A/S23N/A55V/L116F/V128L/V146I/V168L
G6A/S23N/A55V/V128L/V146I/V168L
S23N/A55V/L95I/R134G/N163K/K167T
G6A/A55V/V128L/C130V/V146F/C159A/V168L
G6A/S23N/A55V/L100V/I128L/V146I/V168L
K72E/K83E/R134G/N154K/K167T
LSV/S23N/A55V/I76P/L95V/R134G/N163K/K167T
S23N/A55/I76P/L95V/R134G/N163K/K167T
K83E/R134G/N164D/K167T
G6A/S23N/A55L/L116W/V128L/V146I/V168L
G6A/S23N/A55L/L116W/V128L/V168L
G6A/S23N/A55V/L116W/V128L/V168L
T17N/R134G/N164D/K167T
K72S/K72E/Q94E/Q110E/R134G/N164D/K167T
G6A/S23N/A55V/V128L/V146I/V168L
A55V/R134G/N164D/K167T
G6A/S23N/A55V/V128L/V168L
K2N
S23N
K2E/R134G/N164D/K167T
R134G/N164D/K167T
Q94E/R134G/N164D/K167T
Q110E/R134G/N164D/K167T
Q94E/Q110E/R134G/N164D/K167T
Q94E/Q110E/K142E/N164D/K167T
Q94E/Q110E/R134G/K142E/N164D/K167T
K21T/R134G/N164D/K167T
K72S/R134G/N164D/K167T
G6A/S23T/A55V/V128L/V168L
V17G
R134G/K142R/N164D/K167T
Q94E/Q110E/R134G/K142R/K167T
T17E/R134G/N164D/K167T
R134G/N164D/K167T
Q94E/Q110E/R134G/K142R/N154D
LSV/S23N/A55V/I76P/L95V/F98Y/R134G/N163K/K167T
T15N
G14QA
G6A/S23N/A55V/V128L/C130V/C159A/V168L
R134G/N164D/K167T
G6A/A55V/L95I
G6A/A55V/V128L/V168L
R134G/K167T
G6A/S23N/A55V/V128L/C130V/V146F/C159A/V168L
T17N
K2E
G6A
G6A/A55V
K72E
R134G
K2N
A55V
K166N/K167T
K72Q
R134G/N154D
G6A/A55V/V97I
K167T
V128L
K21N
K27
Q94E/Q110E/K142R/N154D
LSH
V128I
K72S
A102V
V168L
V93I
Wild-Type
V95L
R134G/K142S
Q94E/R134E
Q110E/R134G
R134G/K167T
G394A

FIGURE 13

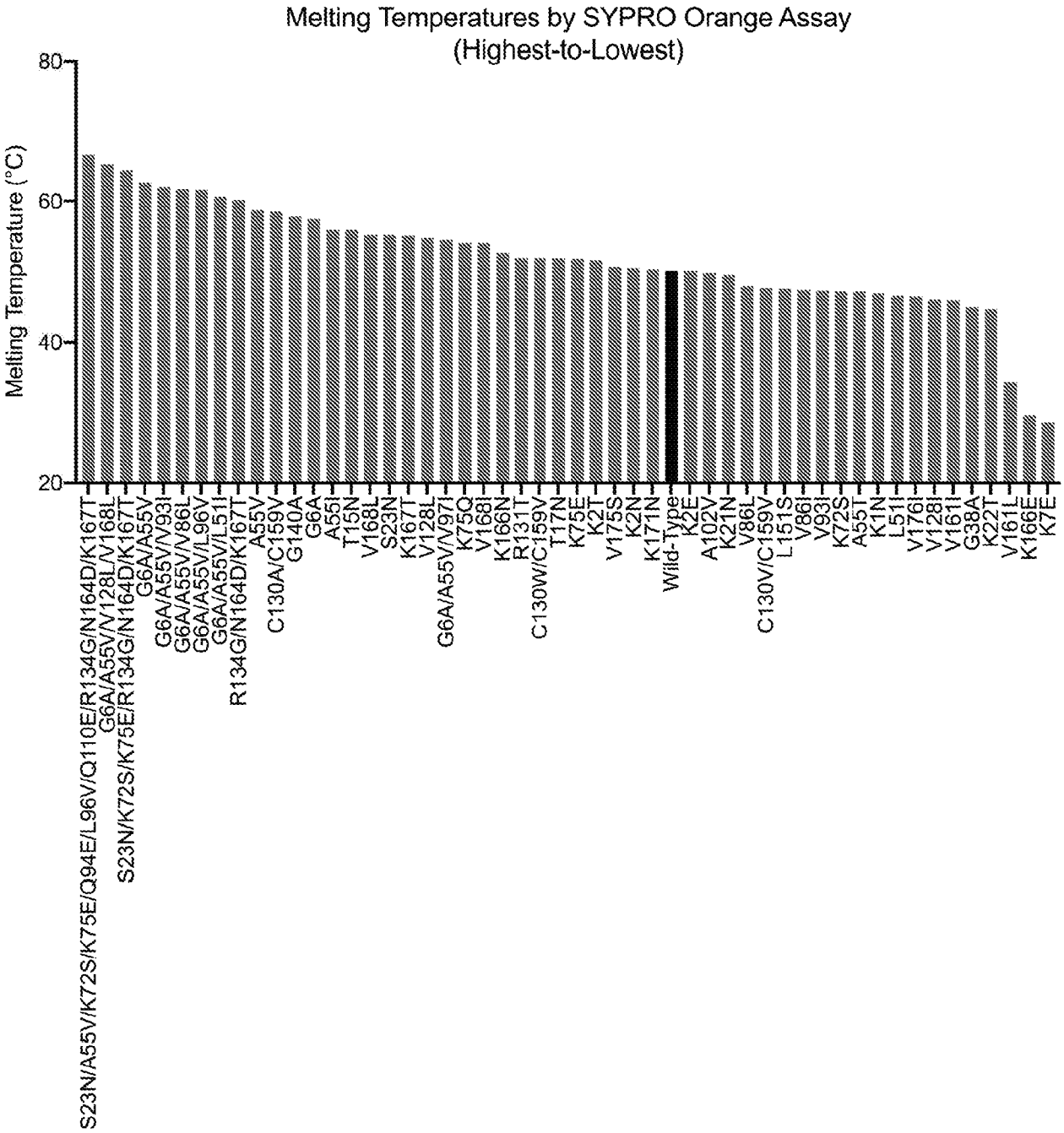

Melting Temperatures by SYPRO Orange Assay
(Highest-to-Lowest)
Melting Temperature (°C)
80
60
40
20
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T
G6A/A55V/V128L/V168L
S23N/K72S/K75E/R134G/N164D/K167T
G6A/A55V
G6A/A55V/V93I
G6A/A55V/V86L
G6A/A55V/L96V
G6A/A55V/L51I
R134G/N164D/K167T
A55V
C130A/C159V
G140A
G6A
A55I
T15N
V168L
S23N
K167T
V128L
G6A/A55V/V97I
K75Q
V168I
K166N
R131T
C130W/C159V
T17N
K75E
K2T
V175S
K2N
K171N
Wild-Type
K2E
A102V
K21N
V86L
C130V/C159V
L151S
V86I
V93I
K72S
A55T
K1N
L51I
V176I
V128I
V161I
G38A
K22T
V161L
K166E
K7E

FIGURE 14

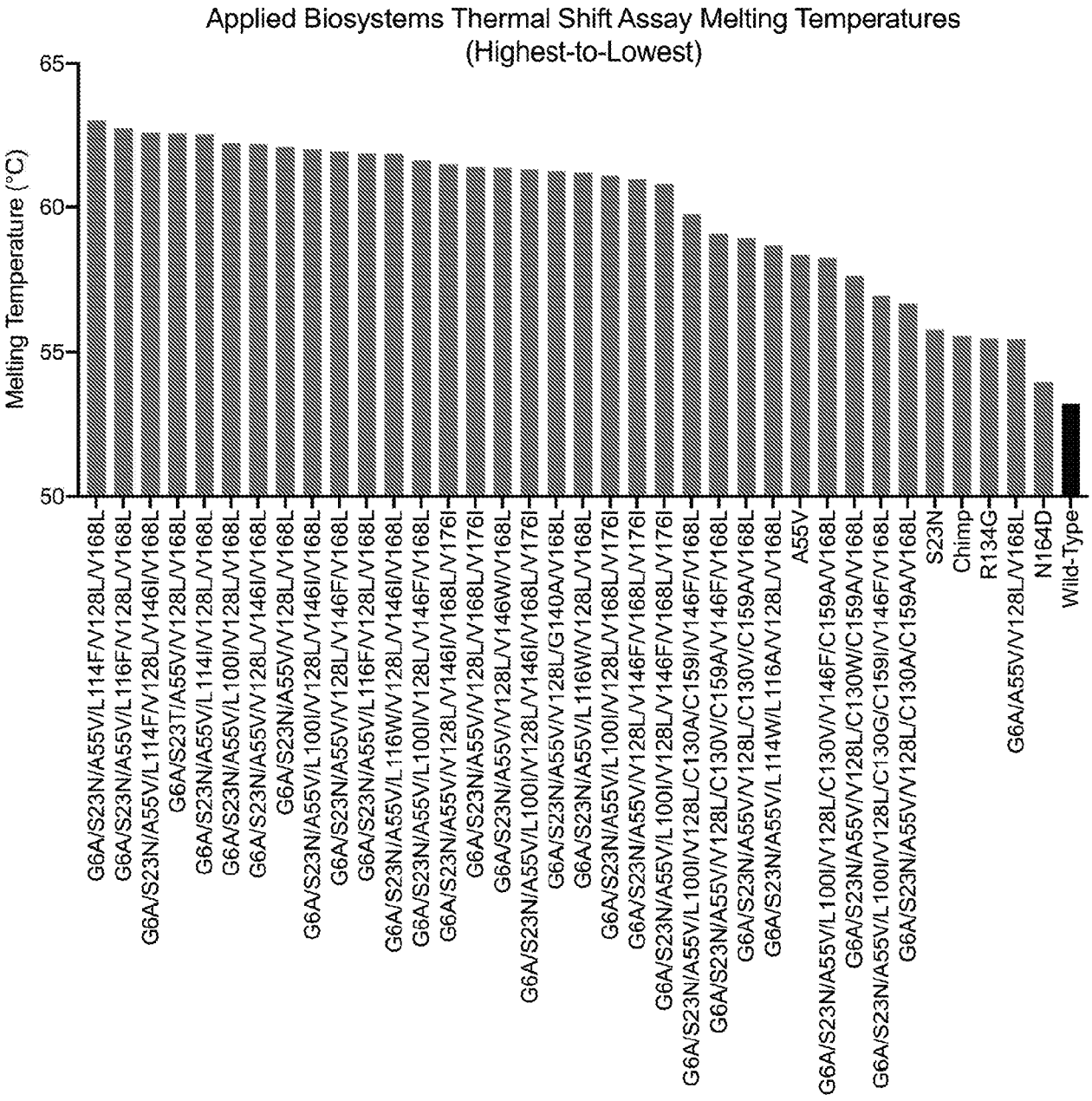

Applied Biosystems Thermal Shift Assay Melting Temperatures
(Highest-to-Lowest)
Melting Temperature (°C)
65
60
55
50
G6A/S23N/A55V/L114F/V128L/V168L
G6A/S23N/A55V/L116F/V128L/V168L
G6A/S23N/A55V/L114F/V128L/V146I/V168L
G6A/S23T/A55V/V128L/V168L
G6A/S23N/A55V/L114I/V128L/V168L
G6A/S23N/A55V/L100I/V128L/V168L
G6A/S23N/A55V/V128L/V146I/V168L
G6A/S23N/A55V/V128L/V168L
G6A/S23N/A55V/L100I/V128L/V146I/V168L
G6A/S23N/A55V/V128L/V146F/V168L
G6A/S23N/A55V/L116F/V128L/V168L
G6A/S23N/A55V/L116W/V128L/V146I/V168L
G6A/S23N/A55V/L100I/V128L/V146F/V168L
G6A/S23N/A55V/V128L/V146I/V168L/V176I
G6A/S23N/A55V/V128L/V168L/V176I
G6A/S23N/A55V/V128L/V146W/V168L
G6A/S23N/A55V/L100I/V128L/V146I/V168L/V176I
G6A/S23N/A55V/V128L/G140A/V168L
G6A/S23N/A55V/L116W/V128L/V168L
G6A/S23N/A55V/L100I/V128L/V168L/V176I
G6A/S23N/A55V/V128L/V146F/V168L/V176I
G6A/S23N/A55V/L100I/V128L/V146F/V168L/V176I
G6A/S23N/A55V/L100I/V128L/C130A/C159I/V146F/V168L
G6A/S23N/A55V/V128L/C130V/C159A/V146F/V168L
G6A/S23N/A55V/V128L/C130V/C159A/V168L
G6A/S23N/A55V/L114W/L116A/V128L/V168L
A55V
G6A/S23N/A55V/L100I/V128L/C130V/V146F/C159A/V168L
G6A/S23N/A55V/V128L/C130W/C159A/V168L
G6A/S23N/A55V/L100I/V128L/C130G/C159I/V146F/V168L
G6A/S23N/A55V/V128L/C130A/C159A/V168L
S23N
Chimp
R134G
G6A/A55V/V128L/V168L
N164D
Wild-Type

FIGURE 15

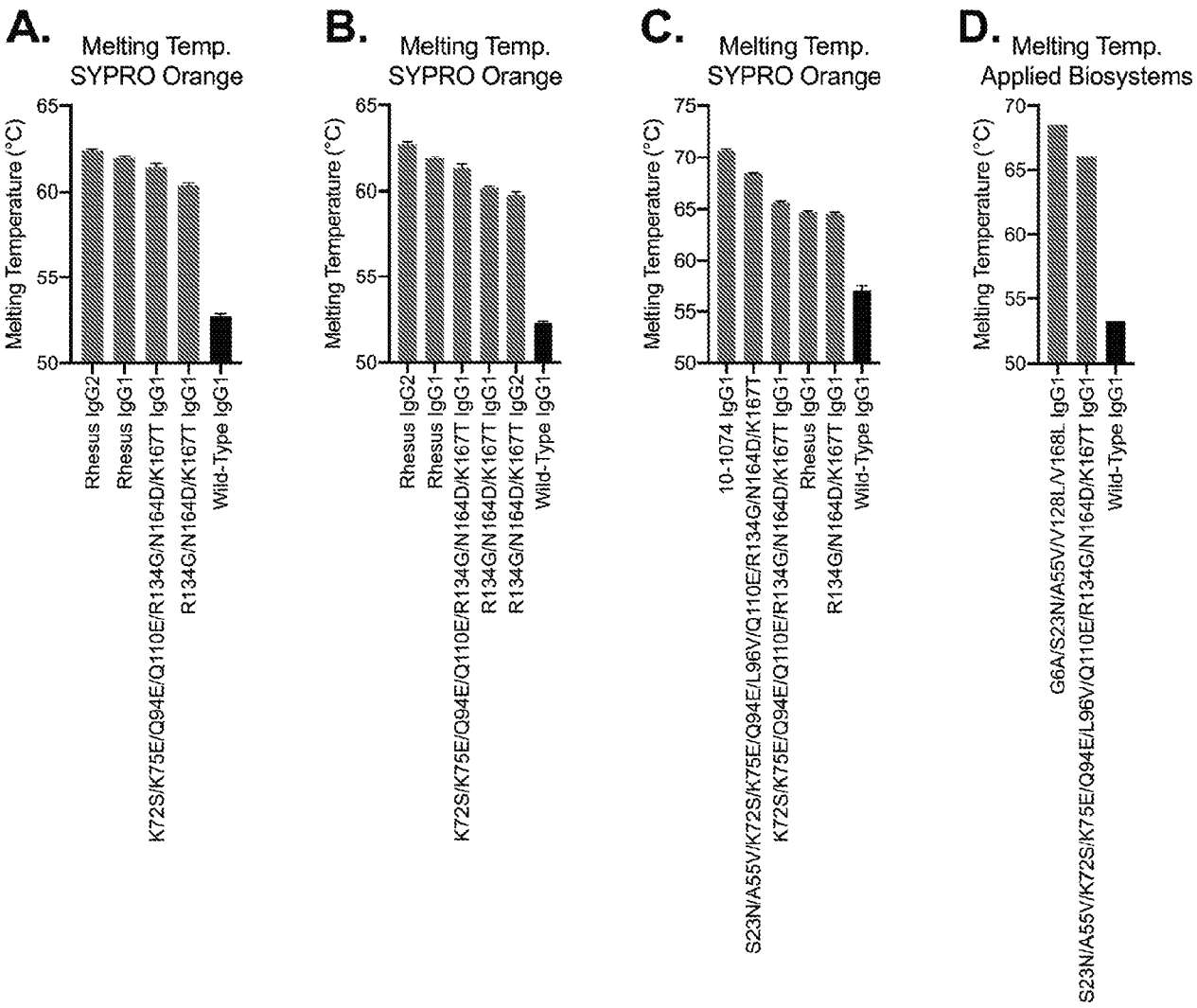

A.
Melting Temp.
SYPRO Orange
Melting Temperature (°C)
65
60
55
50
Rhesus IgG2
Rhesus IgG1
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T IgG1
R134G/N164D/K167T IgG1
Wild-Type IgG1
B.
Melting Temp.
SYPRO Orange
Melting Temperature (°C)
65
60
55
50
Rhesus IgG2
Rhesus IgG1
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T IgG1
R134G/N164D/K167T IgG1
R134G/N164D/K167T IgG2
Wild-Type IgG1
C.
Melting Temp.
SYPRO Orange
Melting Temperature (°C)
75
70
65
60
55
50
10-1074 IgG1
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T IgG1
Rhesus IgG1
R134G/N164D/K167T IgG1
Wild-Type IgG1
D.
Melting Temp.
Applied Biosystems
Melting Temperature (°C)
70
65
60
55
50
G6A/S23N/A55V/V128L/V168L IgG1
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T IgG1
Wild-Type IgG1

FIGURE 16

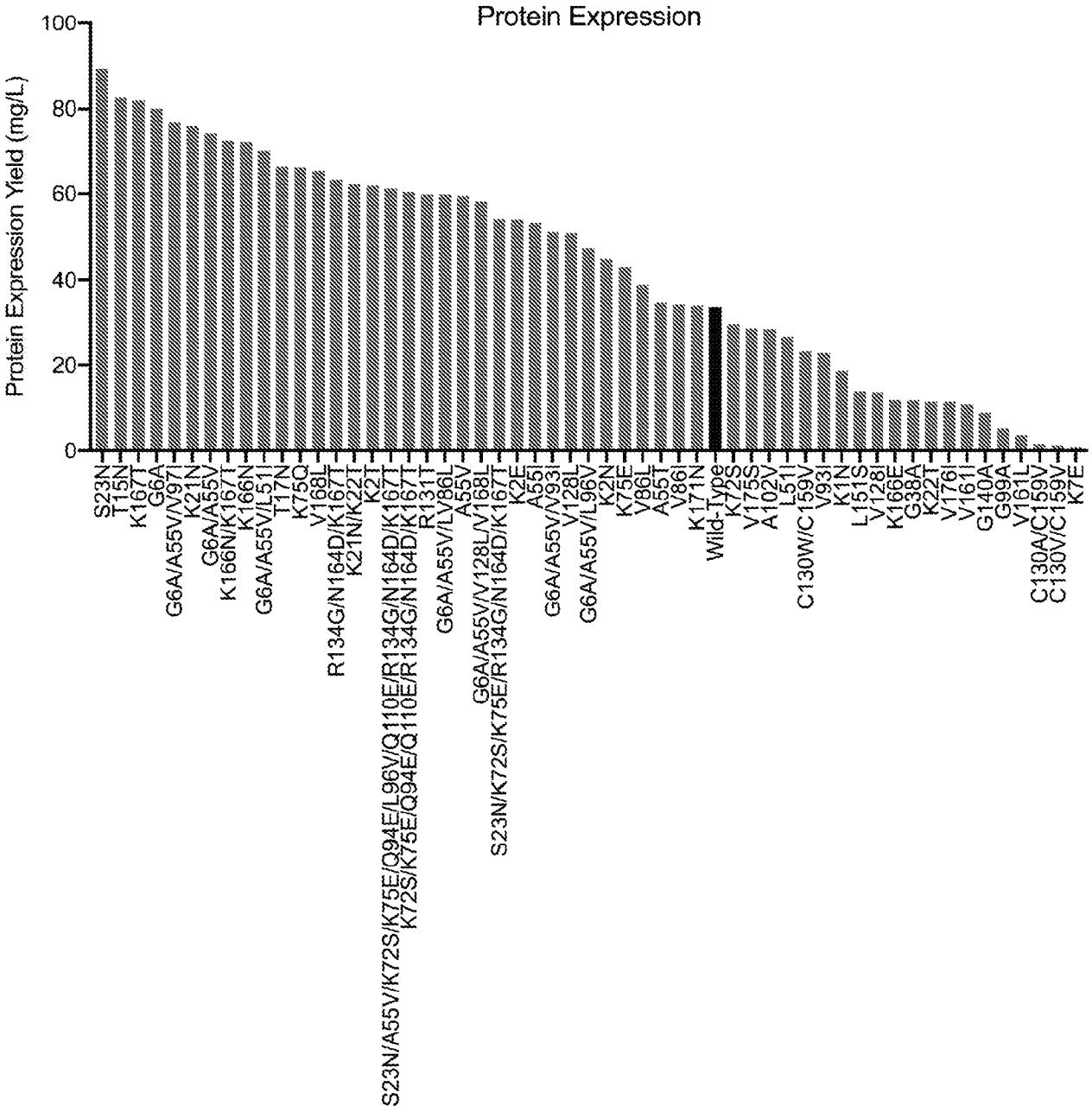

Protein Expression
Protein Expression Yield (mg/L)
100
80
60
40
20
0
S23N
T15N
K167T
G6A
G6A/A55V/V97I
K21N
G6A/A55V
K166N/K167T
K166N
G6A/A55V/L51I
T17N
K75Q
V168L
R134G/N164D/K167T
K21N/K22T
K2T
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T
R131T
G6A/A55V/LV86L
A55V
G6A/A55V/V128L/V168L
S23N/K72S/K75E/R134G/N164D/K167T
K2E
A55I
G6A/A55V/V93I
V128L
G6A/A55V/L96V
K2N
K75E
V86L
A55T
V86I
K171N
Wild-Type
K72S
V175S
A102V
L51I
C130W/C159V
V93I
K1N
L151S
V128I
K166E
G38A
K22T
V176I
V161I
G140A
G99A
V161L
C130A/C159V
C130V/C159V
K7E

FIGURE 17

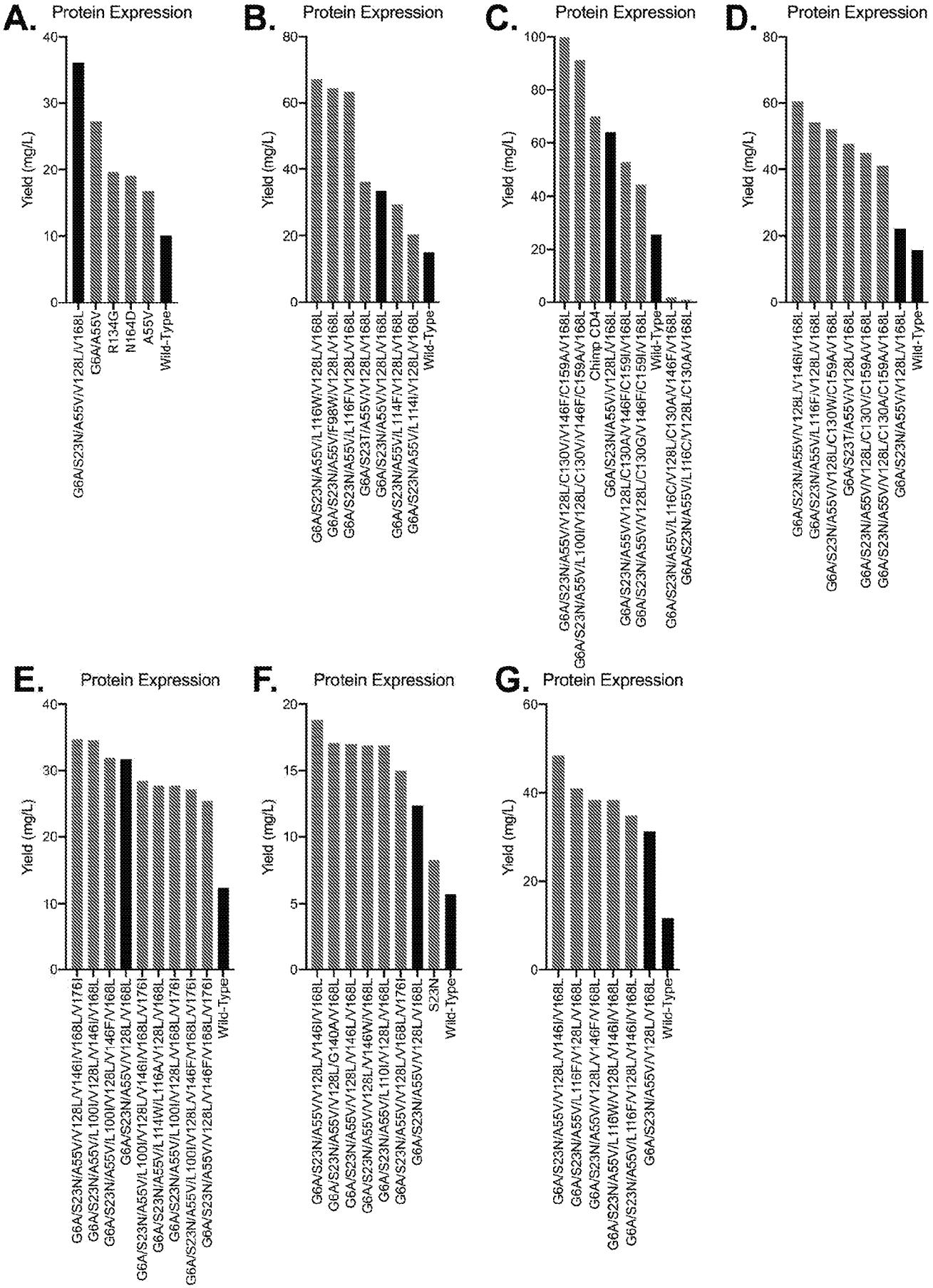

A.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/V128L/V168L
G6A/A55V
R134G
N164D
A55V
Wild-Type
B.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/L116W/V128L/V168L
G6A/S23N/A55V/F98W/V128L/V168L
G6A/S23N/A55V/L116F/V128L/V168L
G6A/S23T/A55V/V128L/V168L
G6A/S23N/A55V/V128L/V168L
G6A/S23N/A55V/L114F/V128L/V168L
G6A/S23N/A55V/L114I/V128L/V168L
Wild-Type
C.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/V128L/C130V/V146F/C159A/V168L
G6A/S23N/A55V/L100I/V128L/C130V/V146F/C159A/V168L
Chimp CD4
G6A/S23N/A55V/V128L/V168L
G6A/S23N/A55V/V128L/C130A/V146F/C159I/V168L
G6A/S23N/A55V/V128L/C130G/V146F/C159I/V168L
Wild-Type
G6A/S23N/A55V/L116C/V128L/C130A/V146F/V168L
G6A/S23N/A55V/L116C/V128L/C130A/V168L
D.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/V128L/V146I/V168L
G6A/S23N/A55V/L116F/V128L/V168L
G6A/S23N/A55V/V128L/C130W/C159A/V168L
G6A/S23T/A55V/V128L/V168L
G6A/S23N/A55V/V128L/C130V/C159A/V168L
G6A/S23N/A55V/V128L/C130A/C159A/V168L
G6A/S23N/A55V/V128L/V168L
Wild-Type
E.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/V128L/V146I/V168L/V176I
G6A/S23N/A55V/L100I/V128L/V146I/V168L
G6A/S23N/A55V/L100I/V128L/V146F/V168L
G6A/S23N/A55V/V128L/V168L
G6A/S23N/A55V/L100I/V128L/V146I/V168L/V176I
G6A/S23N/A55V/L114W/L116A/V128L/V168L
G6A/S23N/A55V/L100I/V128L/V168L/V176I
G6A/S23N/A55V/L100I/V128L/V146F/V168L/V176I
G6A/S23N/A55V/V128L/V146F/V168L/V176I
Wild-Type
F.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/V128L/V146I/V168L
G6A/S23N/A55V/V128L/G140A/V168L
G6A/S23N/A55V/V128L/V146L/V168L
G6A/S23N/A55V/V128L/V146W/V168L
G6A/S23N/A55V/L110I/V128L/V168L
G6A/S23N/A55V/V128L/V168L/V176I
G6A/S23N/A55V/V128L/V168L
S23N
Wild-Type
G.
Protein Expression
Yield (mg/L)
G6A/S23N/A55V/V128L/V146I/V168L
G6A/S23N/A55V/L116F/V128L/V168L
G6A/S23N/A55V/V128L/V146F/V168L
G6A/S23N/A55V/L116W/V128L/V146I/V168L
G6A/S23N/A55V/L116F/V128L/V146I/V168L
G6A/S23N/A55V/V128L/V168L
Wild-Type

FIGURE 17, continued

H.

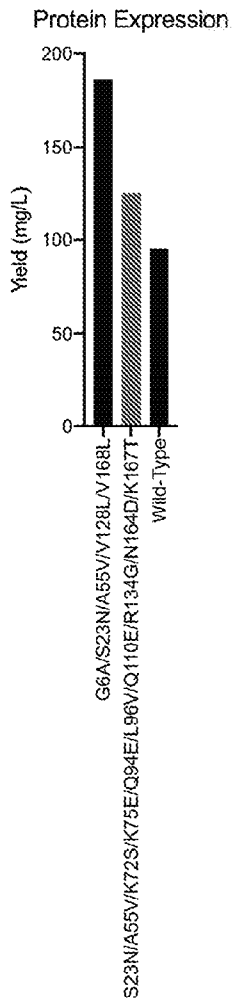


FIGURE 18

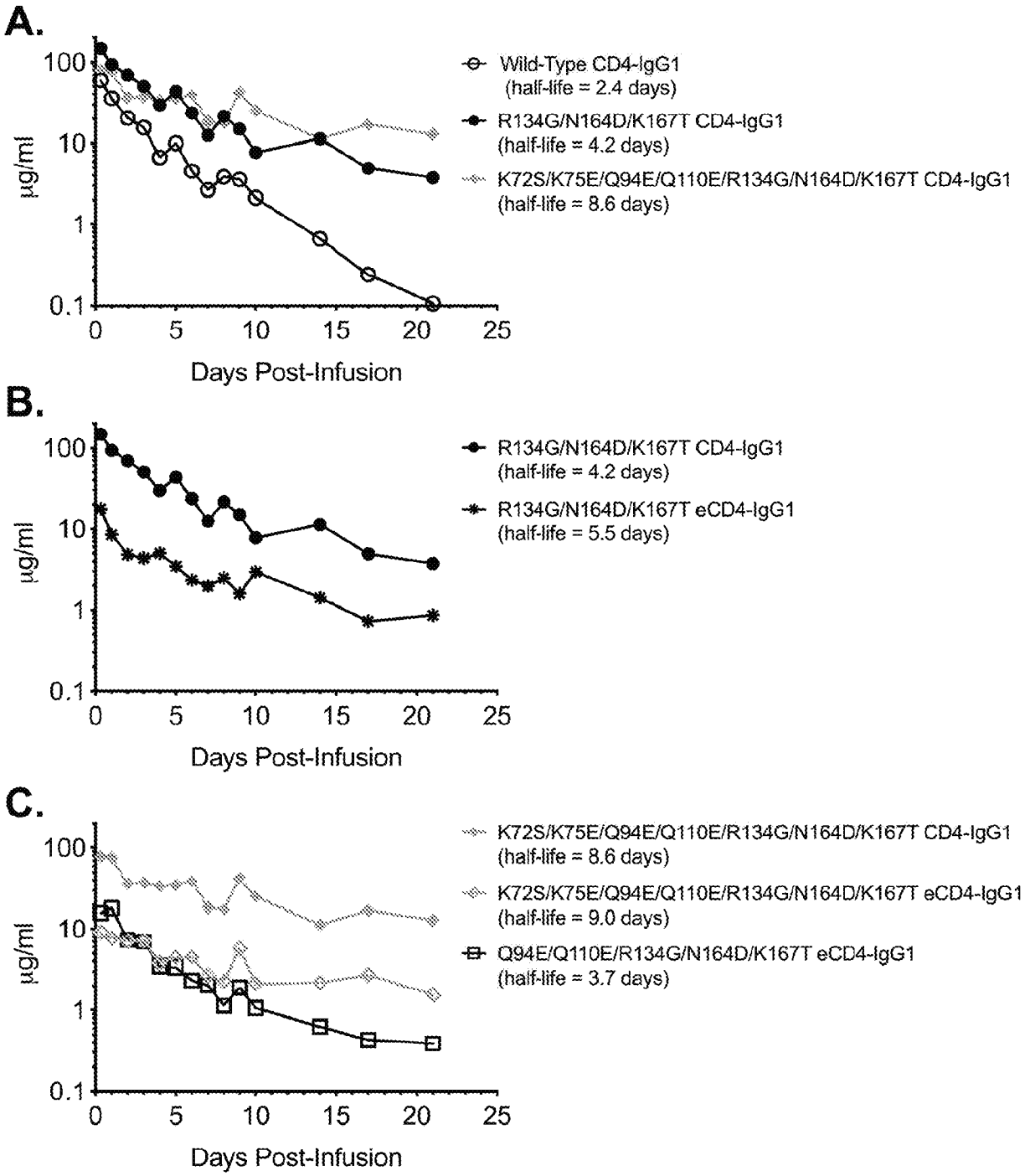

A.
100
10
1
0.1
µg/ml
0
5
10
15
20
25
Days Post-Infusion
Wild-Type CD4-IgG1
(half-life = 2.4 days)
R134G/N164D/K167T CD4-IgG1
(half-life = 4.2 days)
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T CD4-IgG1
(half-life = 8.6 days)
B.
100
10
1
0.1
µg/ml
0
5
10
15
20
25
Days Post-Infusion
R134G/N164D/K167T CD4-IgG1
(half-life = 4.2 days)
R134G/N164D/K167T eCD4-IgG1
(half-life = 5.5 days)
C.
100
10
1
0.1
µg/ml
0
5
10
15
20
25
Days Post-Infusion
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T CD4-IgG1
(half-life = 8.6 days)
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T eCD4-IgG1
(half-life = 9.0 days)
Q94E/Q110E/R134G/N164D/K167T eCD4-IgG1
(half-life = 3.7 days)

FIGURE 19

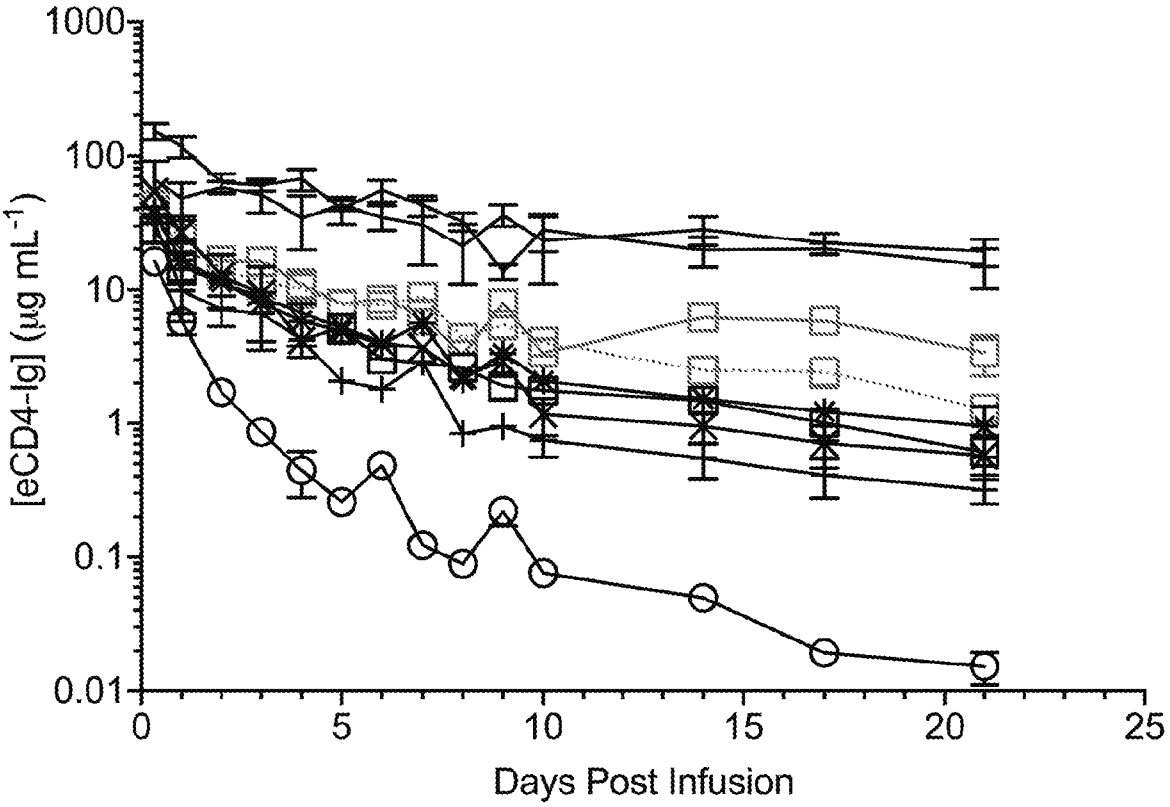
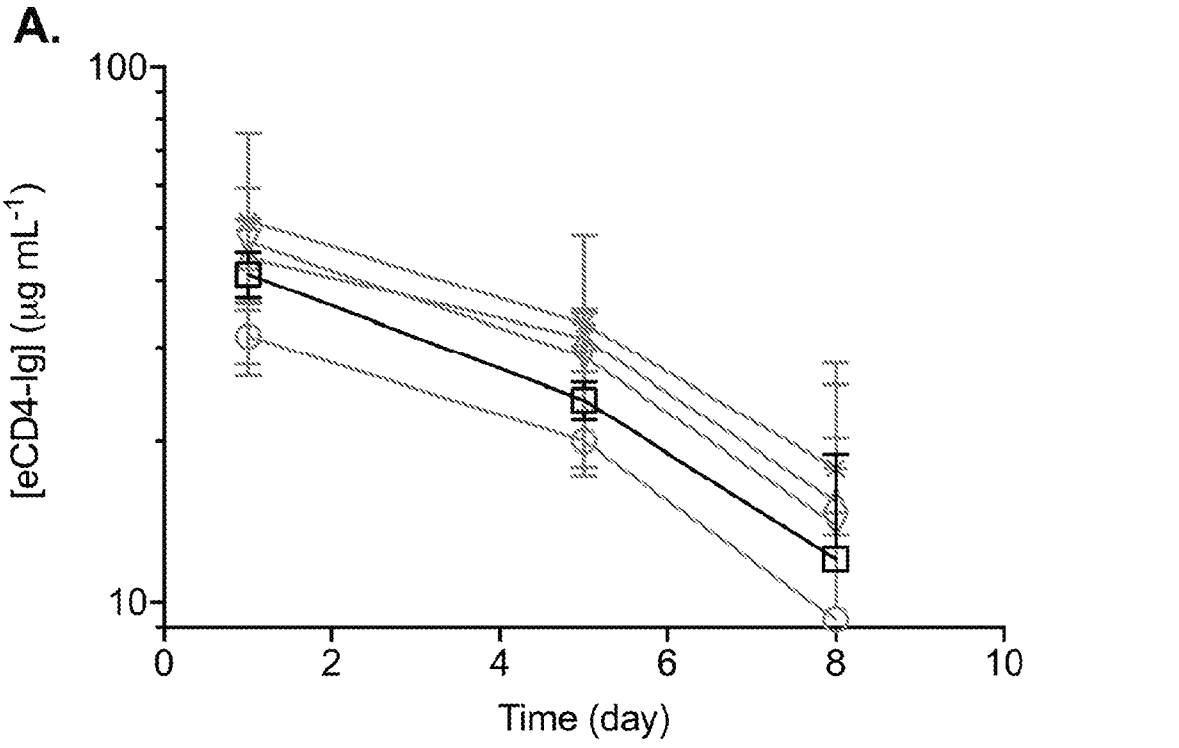

1000
100
10
1
0.1
0.01
[eCD4-Ig] (µg mL-1)
0
5
10
15
20
25
Days Post Infusion
10-1074
Wild-Type
K72S/K75E/R134G/N164D/K167T
K72S/K75E/Q94E/Q110E/R134G/N164D/K167T
S23N/K72S/K75E/R134G/N164D/K167T
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T (LS)
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T (YTE)

FIGURE 20


A.
100
10
[eCD4-Ig] (μg mL-1)
0
2
4
6
8
10
Time (day)
S23N/A55V/K72S/K75E/Q94E/L96V/Q110E/R134G/N164D/K167T
G6A/S23N/A55V/V128L/V168L
G6A/S23N/A55V/V128L/R134G/V168L
G6A/S23N/A55V/V128L/K167T/V168L
G6A/S23N/A55V/V128L/R134G/N164D/K167T/V168L

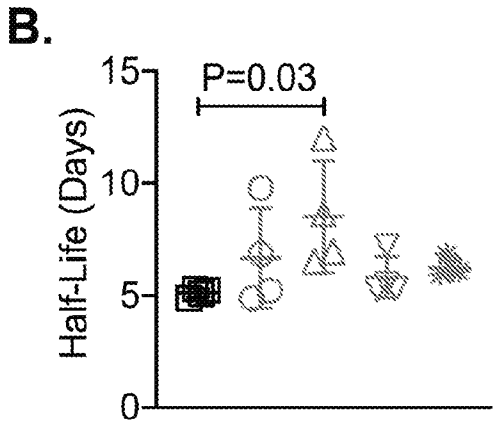

B.
15
10
5
0
Half-Life (Days)
P=0.03

FIGURE 21

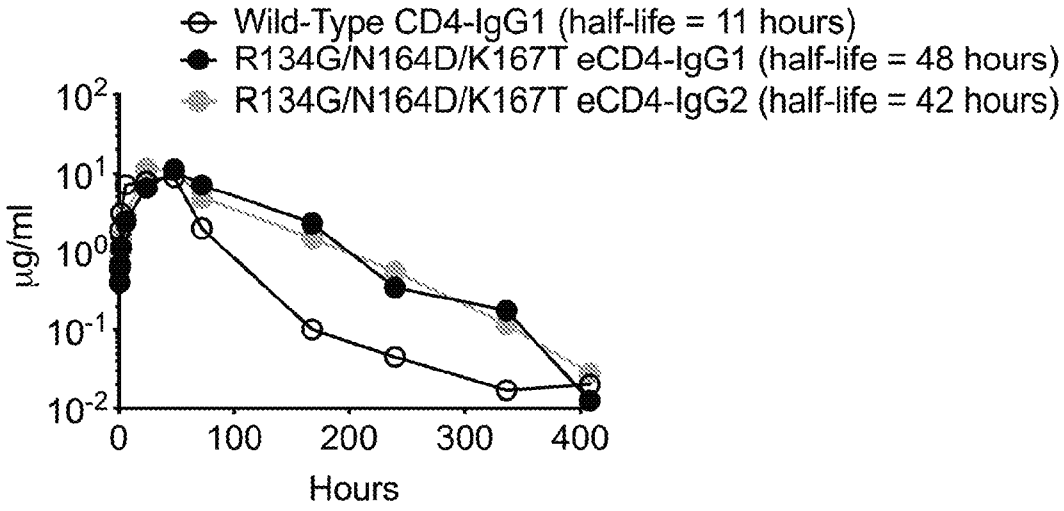

Wild-Type CD4-IgG1 (half-life = 11 hours)
R134G/N164D/K167T eCD4-IgG1 (half-life = 48 hours)
R134G/N164D/K167T eCD4-IgG2 (half-life = 42 hours)
µg/ml
10^2
10^1
10^0
10^-1
10^-2
0
100
200
300
400
Hours

FIGURE 22

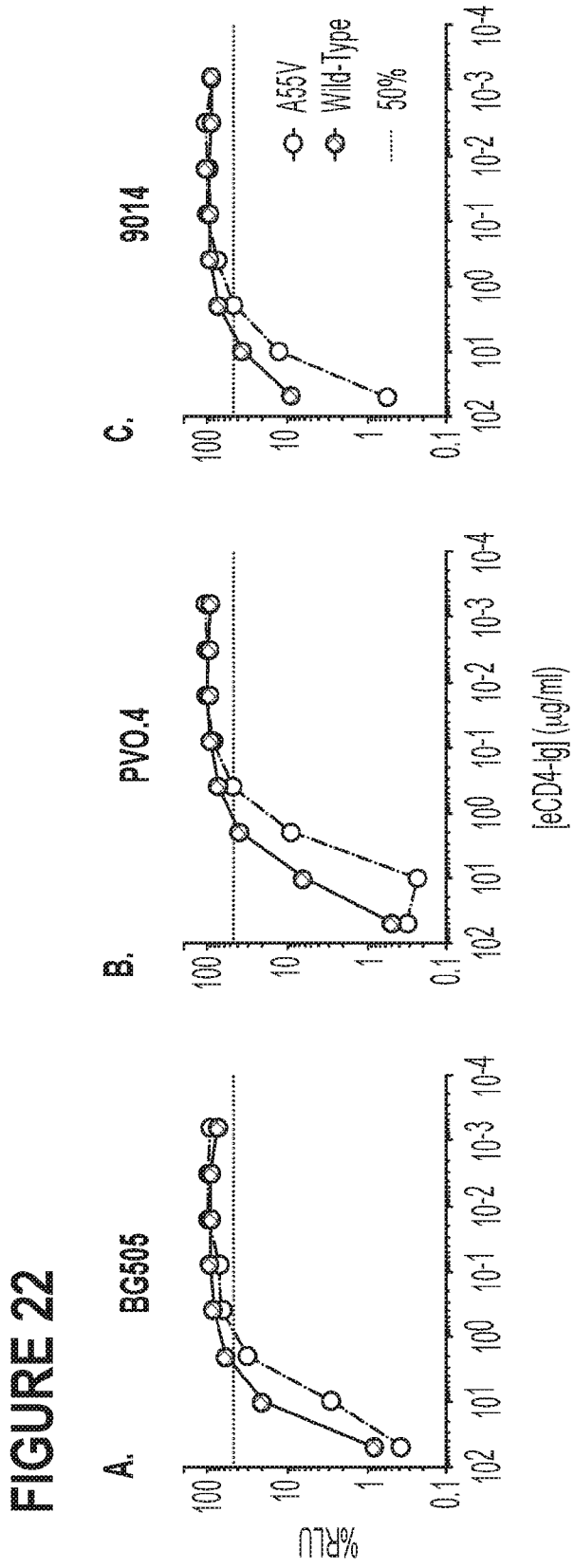

A.
BG505
B.
PVO.4
C.
9014
%RLU
100
10
1
0.1
10-4
10-3
10-2
10-1
100
101
102
A55V
Wild-Type
50%
[eCD4-Ig] (µg/ml)

FIGURE 23

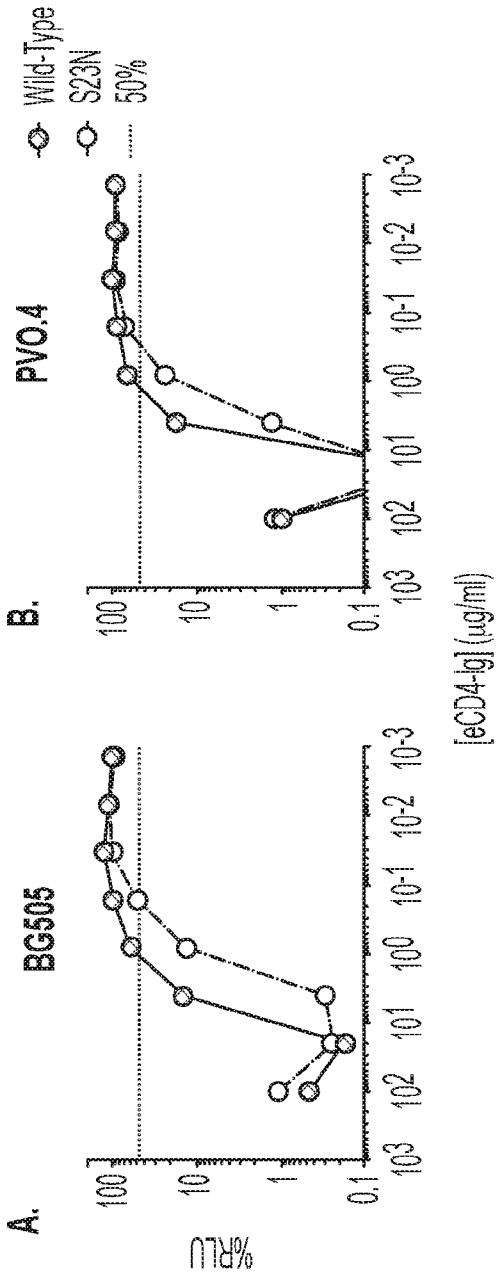

A.
BG505
B.
PVO.4
Wild-Type
S23N
50%
%RLU
100
10
1
0.1
10³
10²
10¹
100
10-1
10-2
10-3
[eCD4-Ig] (µg/ml)

FIGURE 24

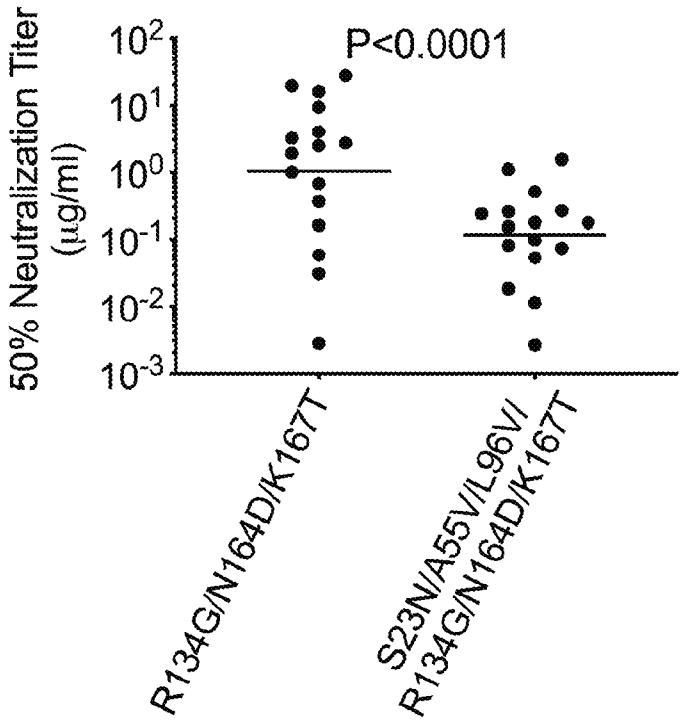

50% Neutralization Titer (μg/ml)
10^2
10^1
10^0
10^{-1}
10^{-2}
10^{-3}
P<0.0001
R134G/N164D/K167T
S23N/A55V/L96V/ R134G/N164D/K167T

FIGURE 25

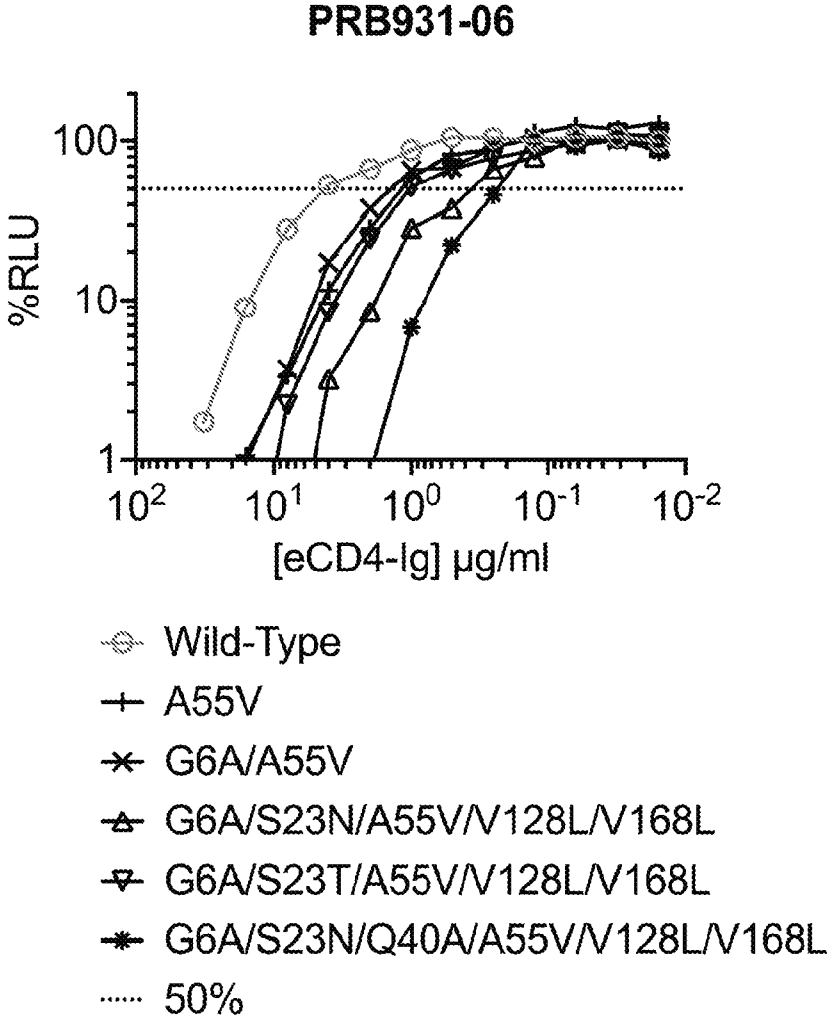

PRB931-06
100
10
1
%RLU
10^2
10^1
10^0
10^{-1}
10^{-2}
[eCD4-Ig] µg/ml
Wild-Type
A55V
G6A/A55V
G6A/S23N/A55V/V128L/V168L
G6A/S23T/A55V/V128L/V168L
G6A/S23N/Q40A/A55V/V128L/V168L
50%

FIGURE 26

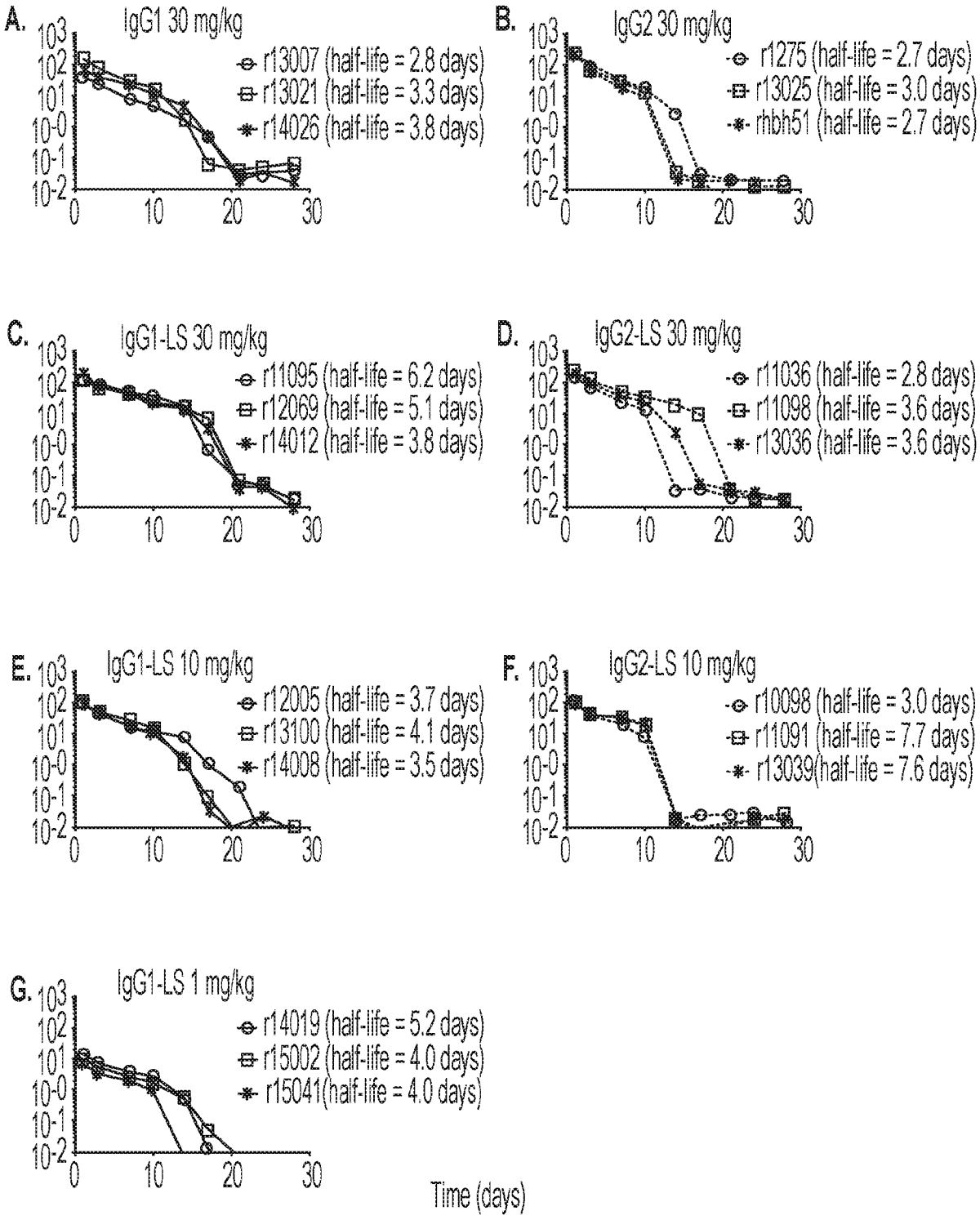
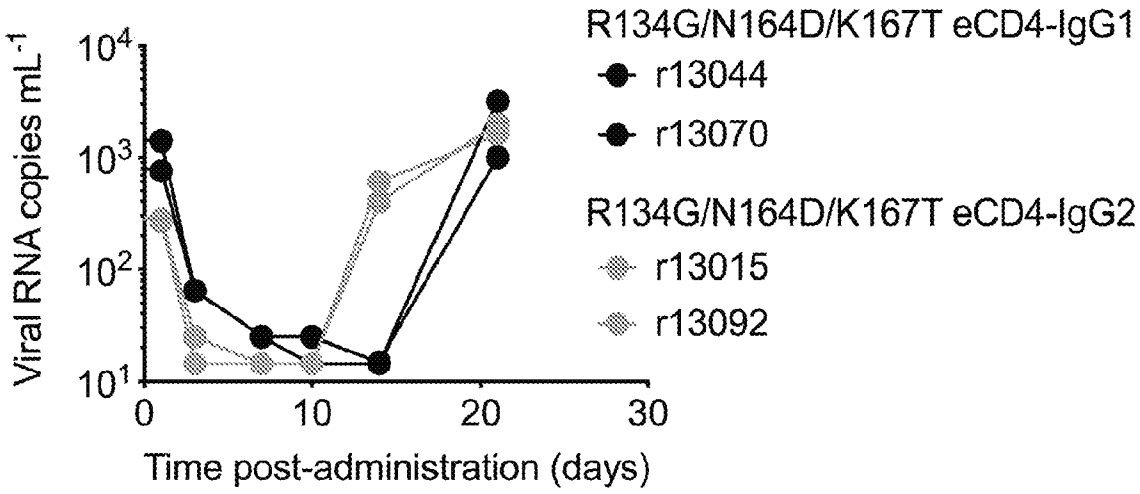

A.
IgG1 30 mg/kg
r13007 (half-life = 2.8 days)
r13021 (half-life = 3.3 days)
r14026 (half-life = 3.8 days)
B.
IgG2 30 mg/kg
r1275 (half-life = 2.7 days)
r13025 (half-life = 3.0 days)
rhbh51 (half-life = 2.7 days)
C.
IgG1-LS 30 mg/kg
r11095 (half-life = 6.2 days)
r12069 (half-life = 5.1 days)
r14012 (half-life = 3.8 days)
D.
IgG2-LS 30 mg/kg
r11036 (half-life = 2.8 days)
r11098 (half-life = 3.6 days)
r13036 (half-life = 3.6 days)
E.
IgG1-LS 10 mg/kg
r12005 (half-life = 3.7 days)
r13100 (half-life = 4.1 days)
r14008 (half-life = 3.5 days)
F.
IgG2-LS 10 mg/kg
r10098 (half-life = 3.0 days)
r11091 (half-life = 7.7 days)
r13039(half-life = 7.6 days)
G.
IgG1-LS 1 mg/kg
r14019 (half-life = 5.2 days)
r15002 (half-life = 4.0 days)
r15041(half-life = 4.0 days)
Time (days)

FIGURE 27


Viral RNA copies mL-1
10^4
10^3
10^2
10^1
0
10
20
30
Time post-administration (days)
R134G/N164D/K167T eCD4-IgG1
r13044
r13070
R134G/N164D/K167T eCD4-IgG2
r13015
r13092