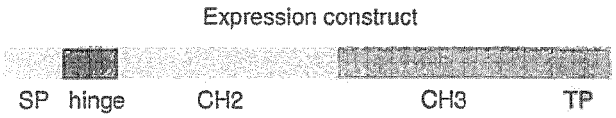
Figure 1


Expression construct
SP
hinge
CH2
CH3
TP

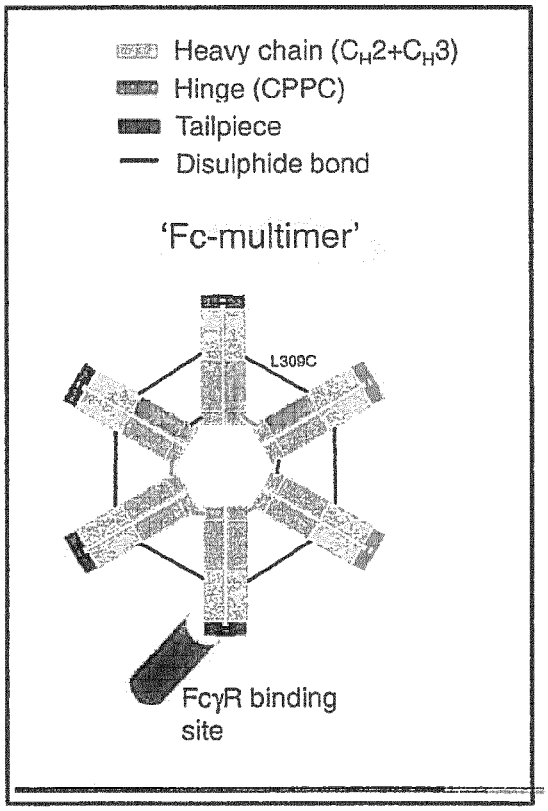

Heavy chain (C_H2+C_H3)
Hinge (CPPC)
Tailpiece
Disulphide bond
'Fc-multimer'
L309C
FcγR binding site

Figure 2a

1. **Human IgG1 Fc-multimer IgM tp L309C** SEQ ID NO: 26

CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVCHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKPTLYNVSLVMSDTAGTCY

2. **Human IgG4 Fc-multimer IgM tp L309C** SEQ ID NO: 27

CPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA
KTKPREEQFNSTYRVVSVLTVCHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY
TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLT
VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKPTLYNVSLVMSDTAGTCY

3. **Human IgG1 Fc-multimer IgA tp L309C** SEQ ID NO: 28

CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVCHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKPTHVNVSVVMAEVDGTCY

4. **Human IgG4 Fc-multimer IgA tp L309C** SEQ ID NO: 29

CPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA
KTKPREEQFNSTYRVVSVLTVCHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY
TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLT
VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKPTHVNVSVVMAEVDGTCY

5. **Human IgG1 Fc-multimer Cμ4-IgM tp L309C** SEQ ID NO: 30

CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVCHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*VALHRPDVYLLPPAREQLNLRESATI*
TCLVTGFSPADVFVQWMQRGQPLSPEKYVTSAPMPEPQAPGRYFAHSILTVSEEEWNTGETY
*TCVAHEALPNRVTERTVDKSTGK*PTLYNVSLVMSDTAGTCY

Figure 2a continued

6. **Human IgG4 Fc-multimer Cμ4-IgM tp L309C** SEQ ID NO: 31

CPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA
KTKPREEQFNSTYRVVSVLTVCHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY
TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLT
VDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK*VALHRPDVYLLPPAREQLNLRESATI*
TCLVTGFSPADVFVQWMQRGQPLSPEKYVTSAPMPEPQAPGRYFAHSILTVSEEEWNTGETY
TCVAHEALPNRVTERTVDKSTGKPTLYNVSLVMSDTAGTCY

7. **Human IgG1 Fc-multimer IgM tp S267A L309C** SEQ ID NO: 32

CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV**A**HEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTV**C**HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKPTLYNVSLVMSDTAGTCY

Figure 2b

IgG1 Fc IgM tp SEQ ID NO: 33

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp SEQ ID NO: 34

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

Figure 2c

IgG1 Fc IgM tp L234F SEQ ID NO: 35

CPPCPAPE**F**L GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG1 Fc IgM tp L234F P331S SEQ ID NO: 36

CPPCPAPE**F**L GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPA**S**IEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp F234L SEQ ID NO: 37

CPPCPAPE**L**L GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp F234L F296Y SEQ ID NO: 38

CPPCPAPE**L**L GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ **Y**NSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

Figure 2c continued

IgG4 Fc IgM tp G327A S330A SEQ ID NO: 39

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN K**A**LP**A**SIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp G327A S331P SEQ ID NO: 40

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN K**A**LPS**P**IEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp S330A S331P SEQ ID NO: 41

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLP**AP**IEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

Figure 2d

IgG1 CH2 IgG4 CH3 IgM tp SEQ ID NO: 42

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 CH2 IgG1 CH3 IgM tp SEQ ID NO: 43

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 2e

IgG4 CH2 / IgG1 CH3 hybrid IgM tp F234L SEQ ID NO: 44

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 CH2 / IgG1 CH3 hybrid IgM tp G327A S331P SEQ ID NO: 45

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPSPIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 CH2 / IgG1 CH3 hybrid IgM tp F234L F296Y SEQ ID NO: 46

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 2e continued

IgG4 CH2 / IgG1 CH3 hybrid IgM tp G327A S330A SEQ ID NO: 47

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPASIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 2f

(i)

atggaatggtcctgggtcttcctgtttttcctttctgtcacaaccggggtgcacagc

SEQ ID NO: 48

(ii)

MEWSWVFLFFLSVTTGVHS SEQ ID NO: 49

Figure 2g

IgG1 Fc IgM tp L309C SEQ ID NO: 50

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp L309C SEQ ID NO: 51

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG1 Fc IgM tp L309C L234F SEQ ID NO: 52

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG1 Fc IgM tp L309C L234F P331S SEQ ID NO: 53

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPASIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 2q continued

IgG4 Fc IgM tp L309C F234L SEQ ID NO: 54

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp L309C F234L F296Y SEQ ID NO: 55

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp L309C G327A S330A SEQ ID NO: 56

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPASIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 Fc IgM tp L309C G327A S331P SEQ ID NO: 57

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPSPIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

Figure 2g continued

IgG4 Fc IgM tp L309C S330A S331P SEQ ID NO: 58

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPAPIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG1 CH2 IgG4 CH3 IgM tp L309C SEQ ID NO: 59

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQ
PRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSRLTVDKS RWQEGNVFSC SVMHEALHNH YTQKSLSLSL GKPTLYNVSL VMS
DTAGTCY

IgG4 CH2 IgG1 CH3 IgM tp L309C SEQ ID NO: 60

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 2g continued

IgG4 CH2 / IgG1 CH3 hybrid IgM tp L309C F234L SEQ ID NO: 61

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 CH2 / IgG1 CH3 hybrid IgM tp L309C G327A S331P SEQ ID NO: 62

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPSPIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

IgG4 CH2 / IgG1 CH3 hybrid IgM tp L309C F234L F296Y SEQ ID NO: 63

CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ YNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 2g continued

IgG4 CH2 / IgG1 CH3 hybrid IgM tp L309C G327A S330A SEQ ID NO: 64

CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEV
H NAKTKPREEQ FNSTYRVVSV LTVCHQDWLN GKEYKCKVSN KALPASIEKT ISKAKGQ
PRE PQVYTLPPSR DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTP PVLDS
DGSFF LYSKLTVDKS RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GKPTLYNVSL VMS
DTAGTCY

Figure 3(a)

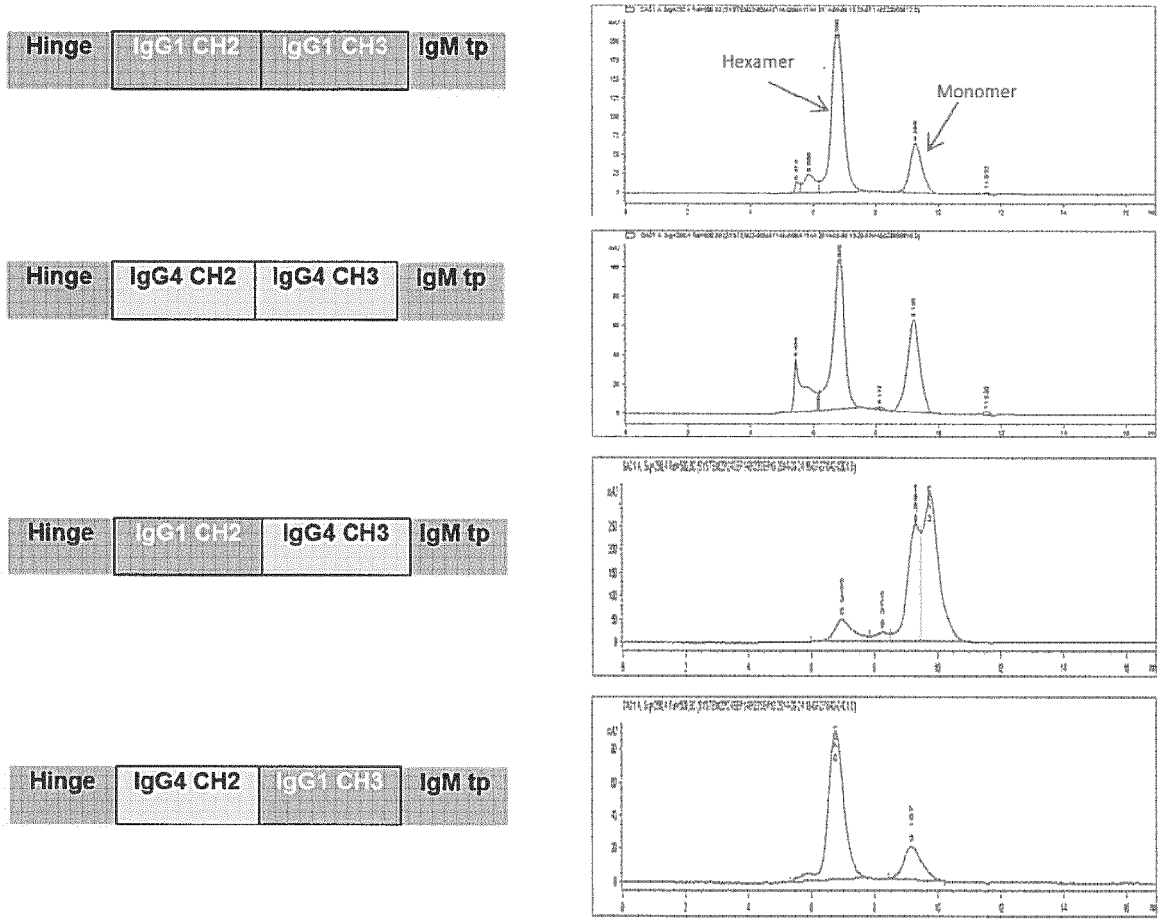

Hinge
IgG1 CH2
IgG1 CH3
IgM tp
Hexamer
Monomer
Hinge
IgG4 CH2
IgG4 CH3
IgM tp
Hinge
IgG1 CH2
IgG4 CH3
IgM tp
Hinge
IgG4 CH2
IgG1 CH3
IgM tp

Figure 3(b)

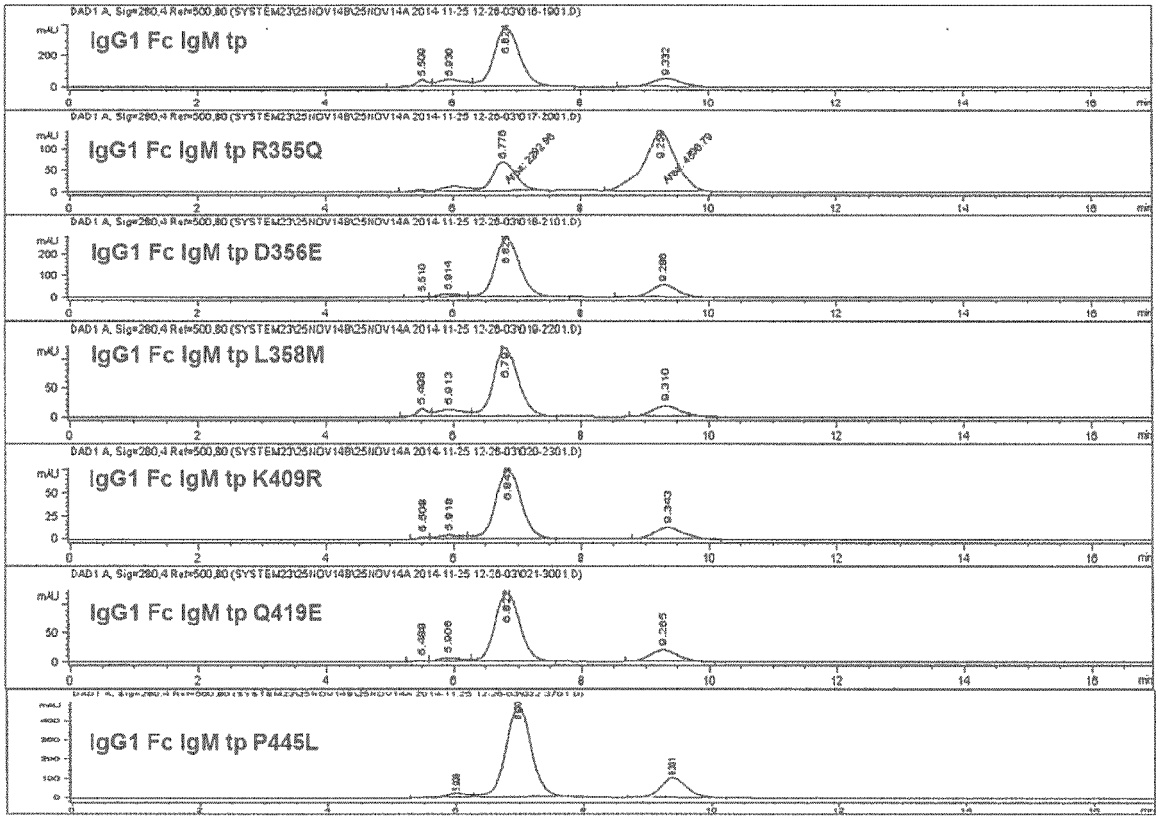

IgG1 Fc IgM tp
IgG1 Fc IgM tp R355Q
IgG1 Fc IgM tp D356E
IgG1 Fc IgM tp L358M
IgG1 Fc IgM tp K409R
IgG1 Fc IgM tp Q419E
IgG1 Fc IgM tp P445L

Figure 3(c)

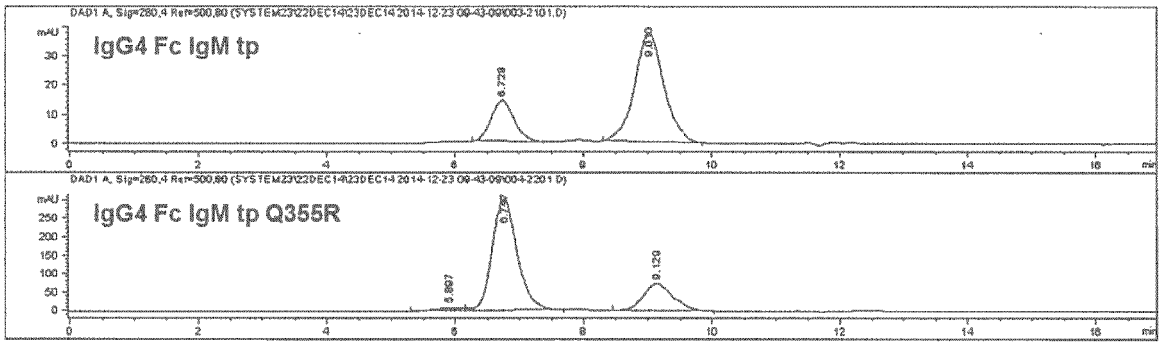


Figure 3(d)

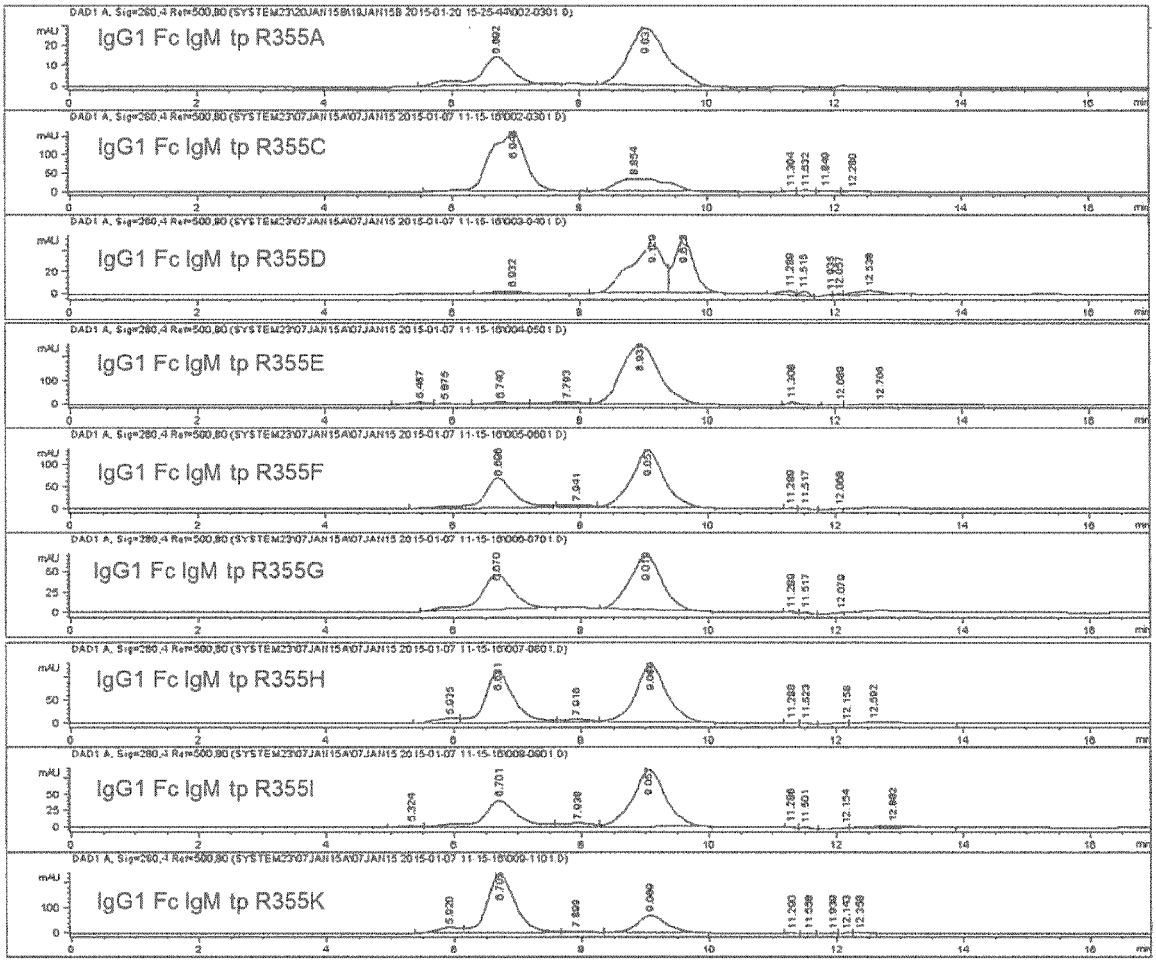

IgG1 Fc IgM tp R355A
IgG1 Fc IgM tp R355C
IgG1 Fc IgM tp R355D
IgG1 Fc IgM tp R355E
IgG1 Fc IgM tp R355F
IgG1 Fc IgM tp R355G
IgG1 Fc IgM tp R355H
IgG1 Fc IgM tp R355I
IgG1 Fc IgM tp R355K

Figure 3(d) continued

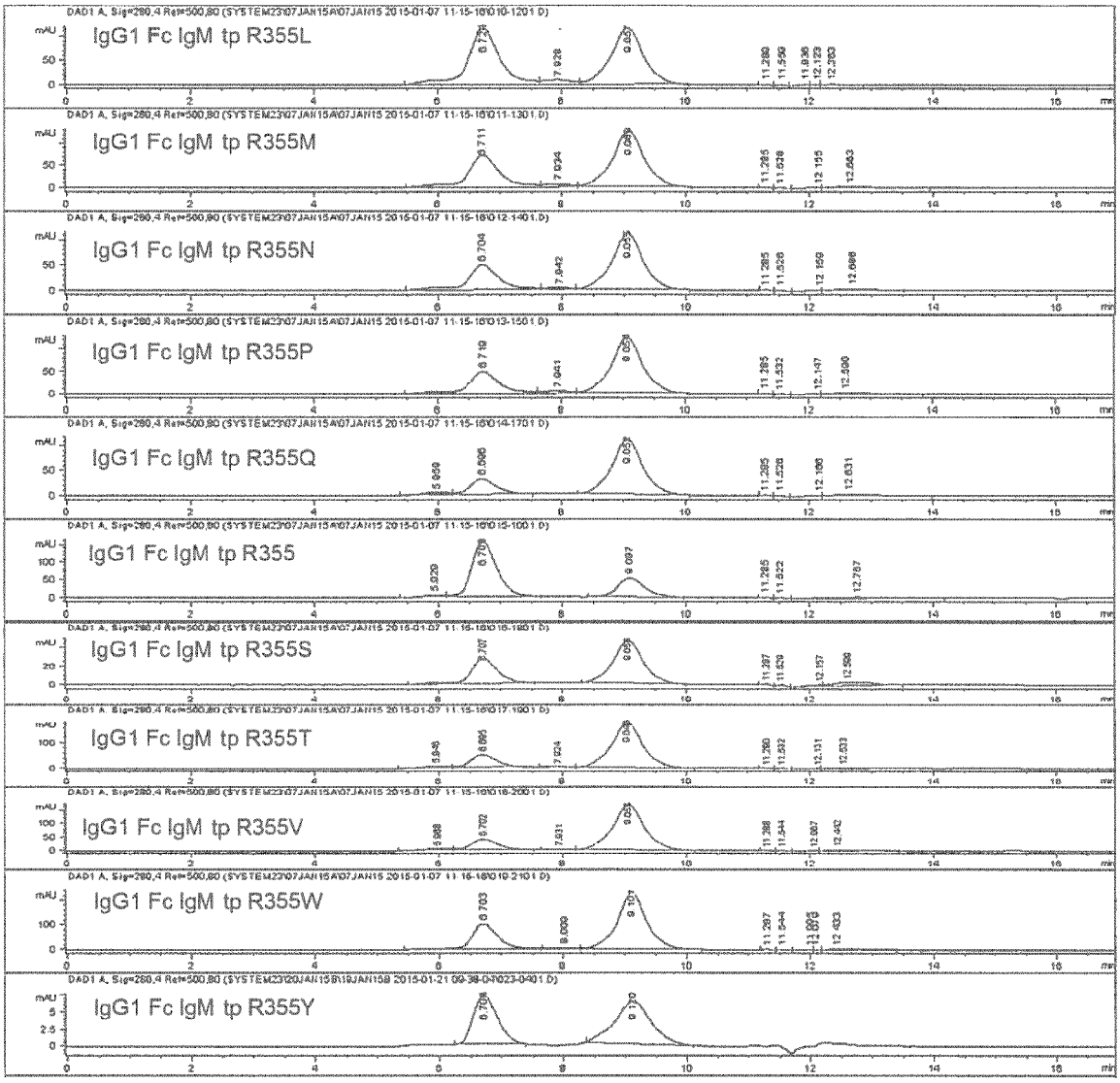
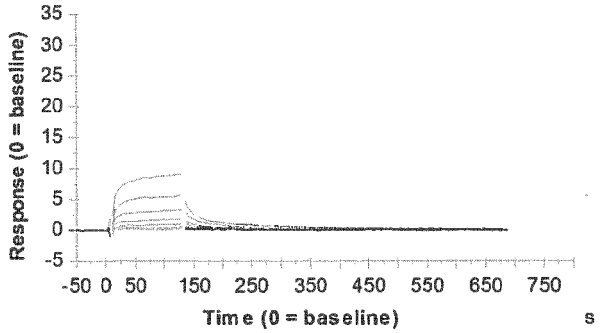
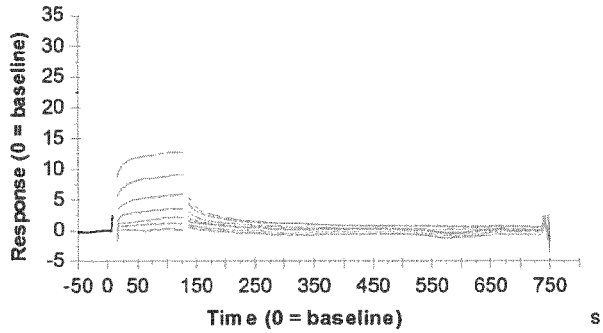


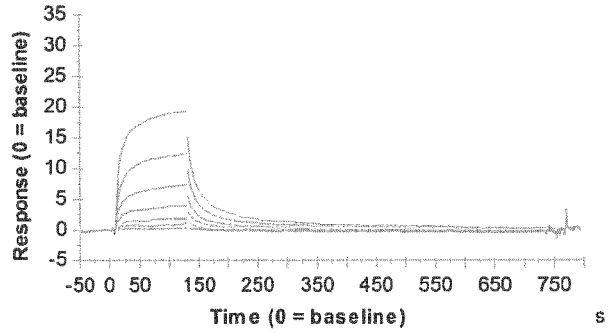
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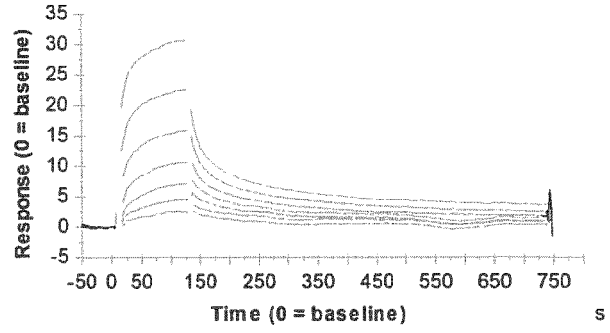
(a)



(b)

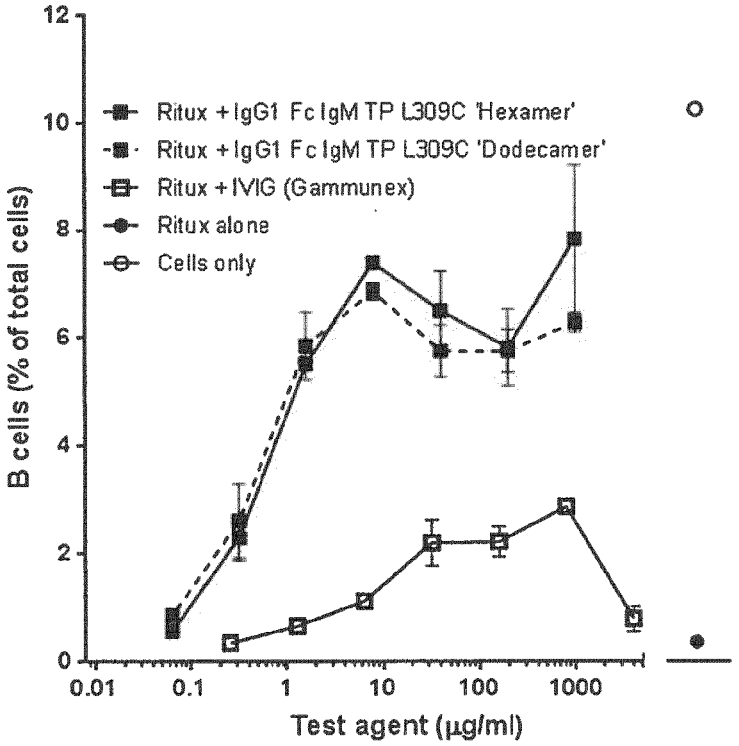


(c)



(d)

Figure 5


Ritux + IgG1 Fc IgM TP L309C 'Hexamer'
Ritux + IgG1 Fc IgM TP L309C 'Dodecamer'
Ritux + IVIG (Gammunex)
Ritux alone
Cells only
B cells (% of total cells)
Test agent (µg/ml)
0.01
0.1
1
10
100
1000

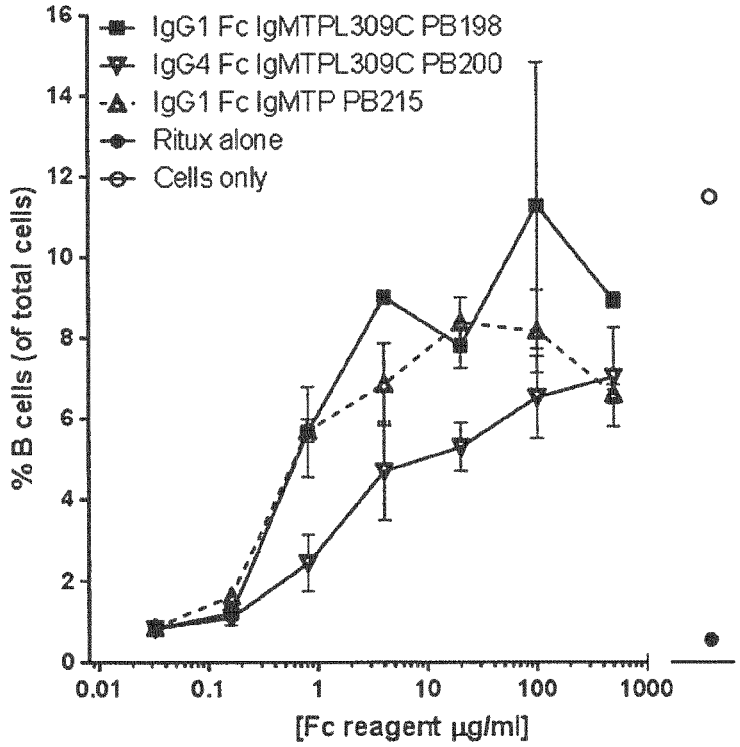
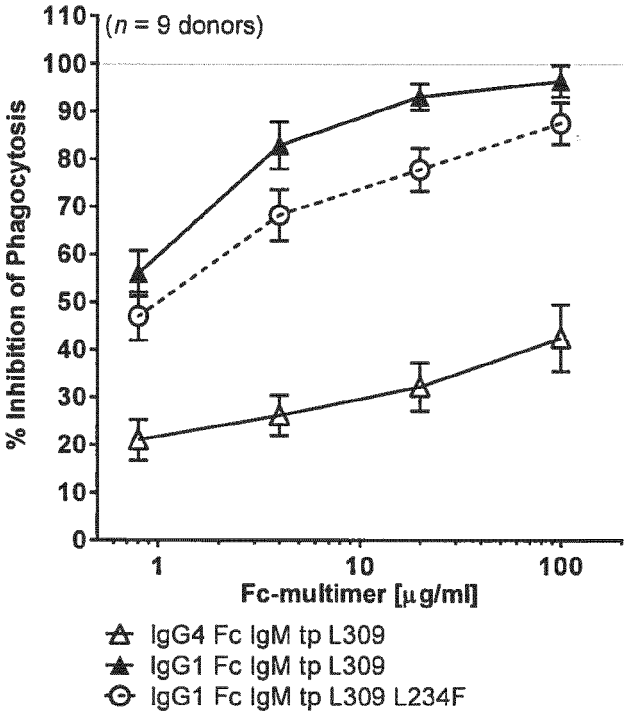

IgG1 Fc IgMTPL309C PB198
IgG4 Fc IgMTPL309C PB200
IgG1 Fc IgMTP PB215
Ritux alone
Cells only
% B cells (of total cells)
[Fc reagent µg/ml]
0.01
0.1
1
10
100
1000

Figure 6


(n = 9 donors)
% Inhibition of Phagocytosis
110
100
90
80
70
60
50
40
30
20
10
0
1
10
100
Fc-multimer [µg/ml]
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309
IgG1 Fc IgM tp L309 L234F

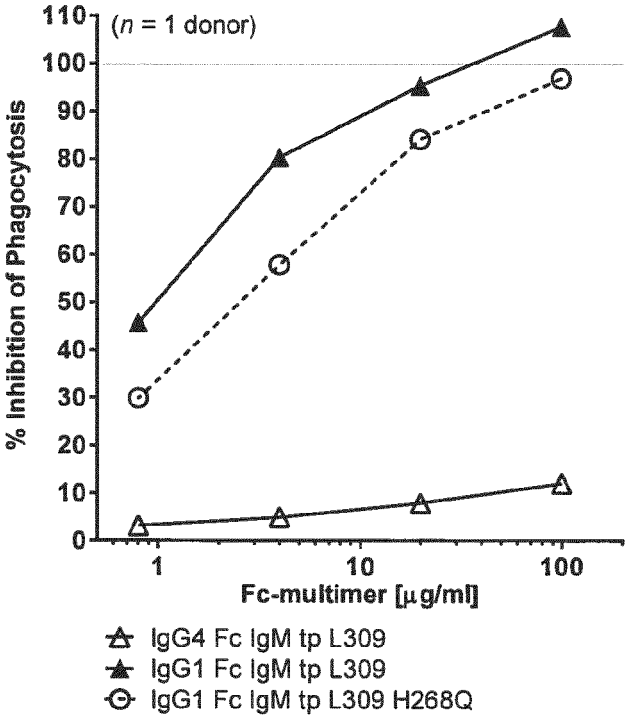
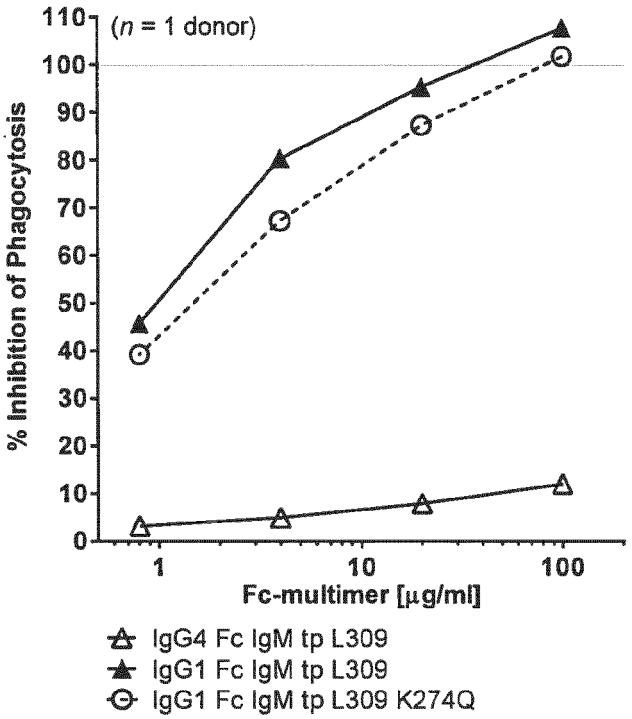

(n = 1 donor)
% Inhibition of Phagocytosis
110
100
90
80
70
60
50
40
30
20
10
0
1
10
100
Fc-multimer [µg/ml]
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309
IgG1 Fc IgM tp L309 H268Q

Figure 6 continued



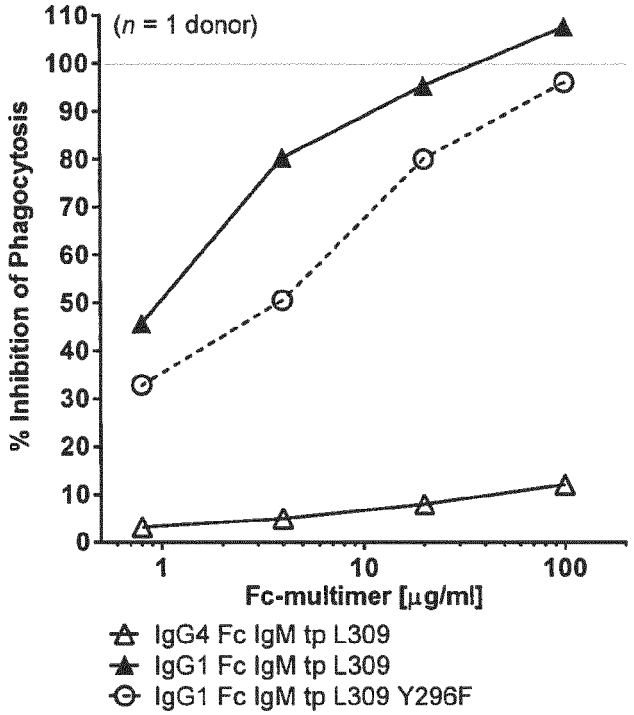
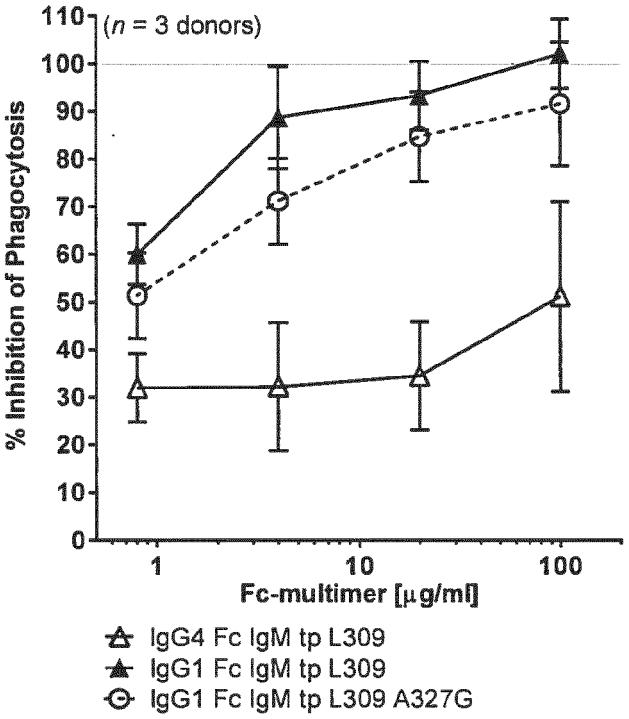


Figure 6 continued



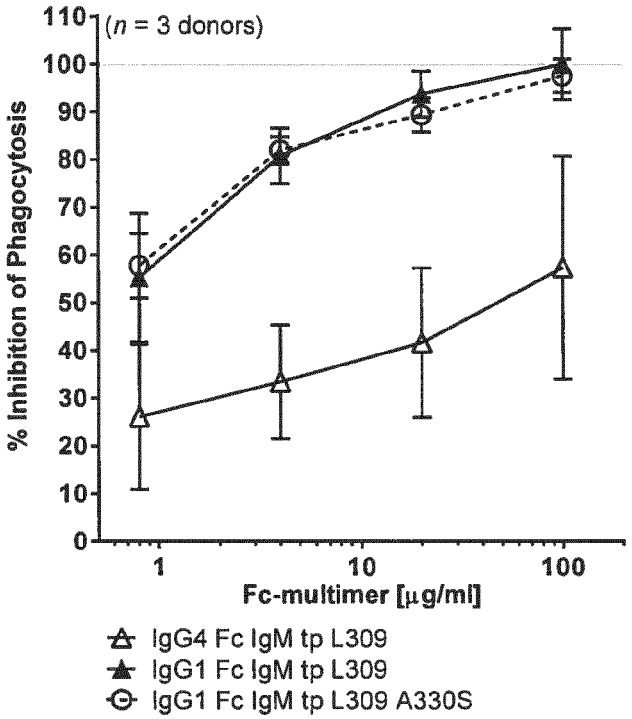
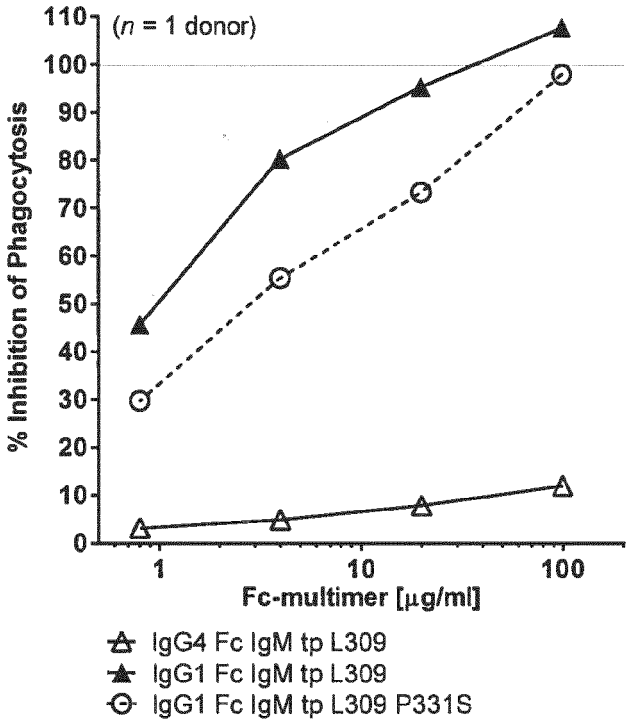


Figure 6 continued



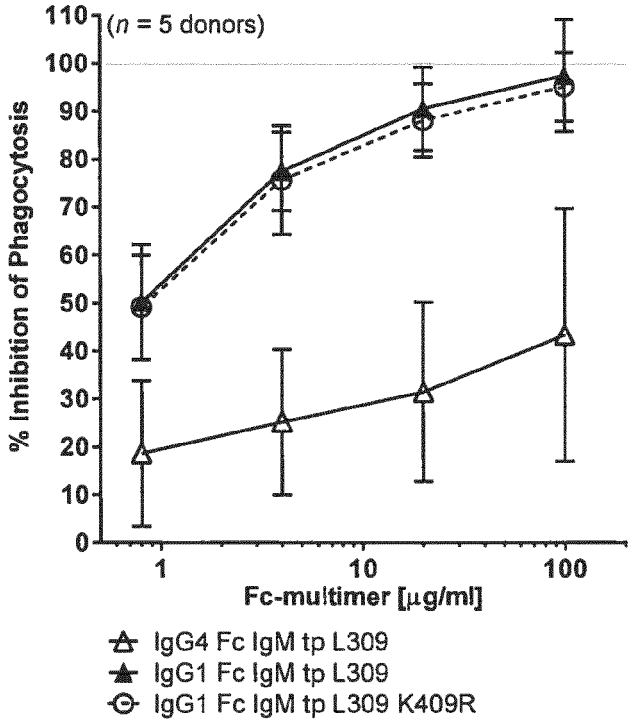
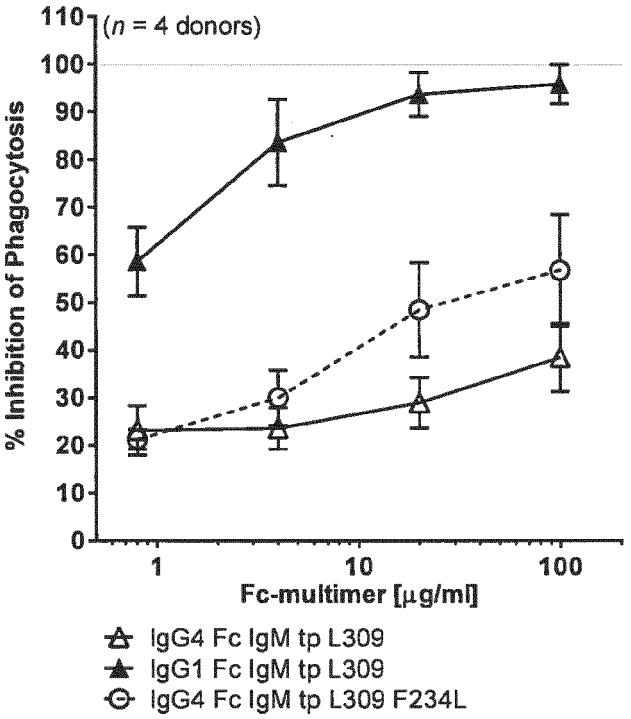


Figure 6 continued



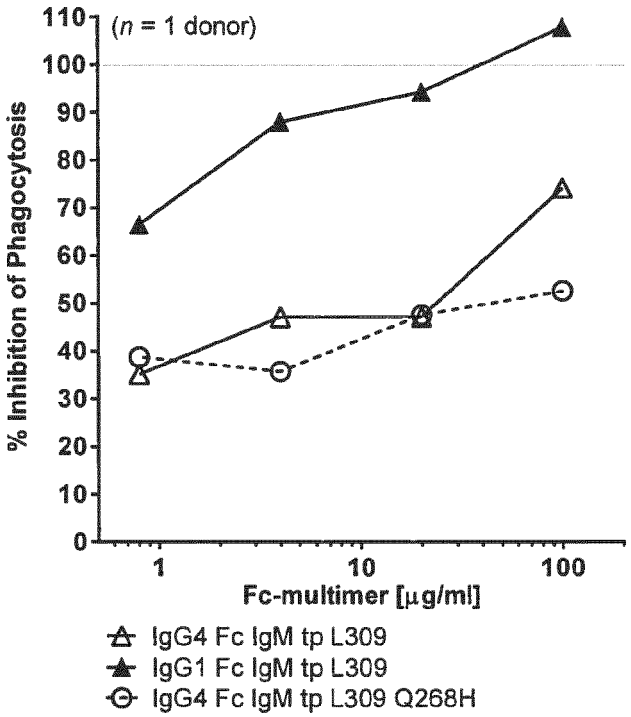
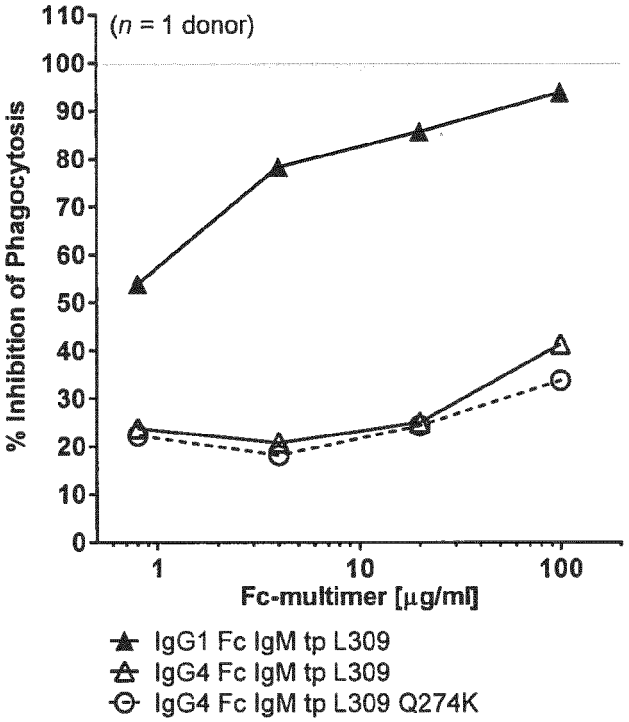


Figure 6 continued



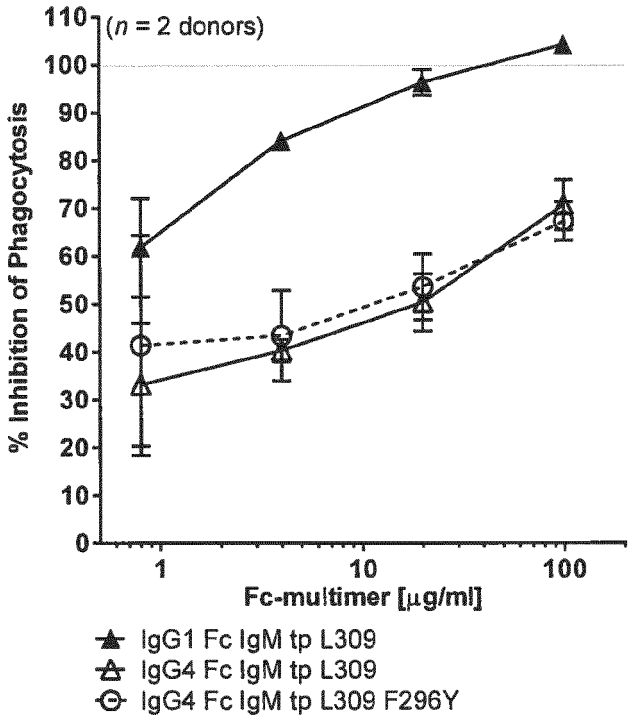
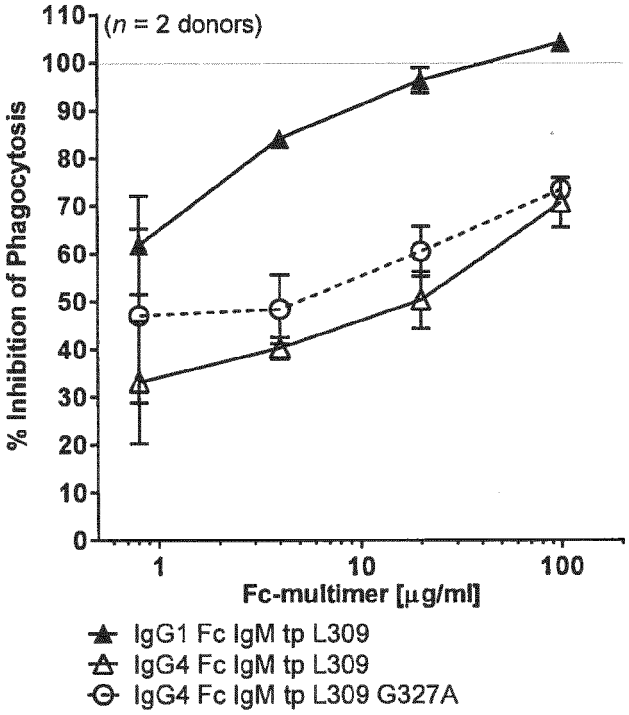


Figure 6 continued



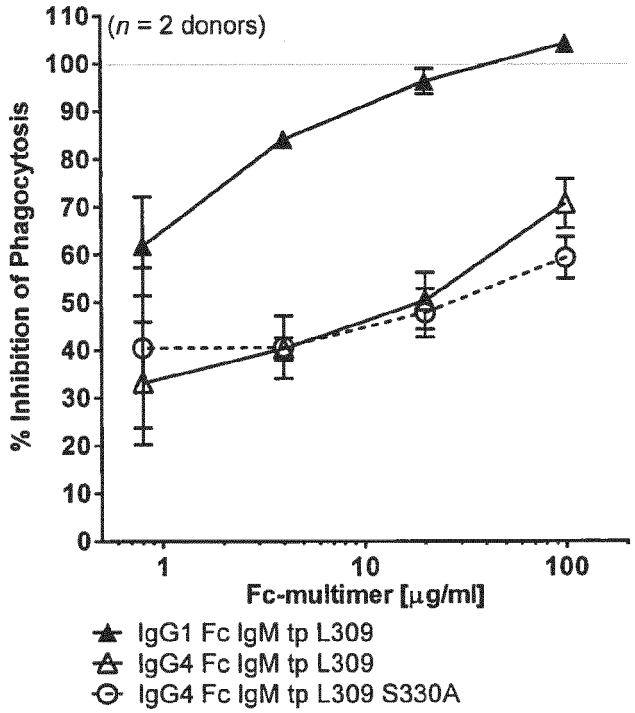
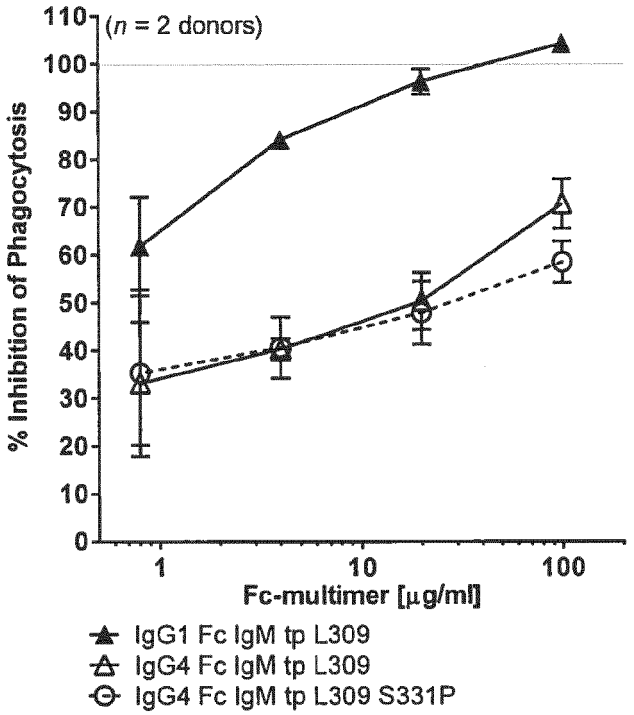


Figure 6 continued



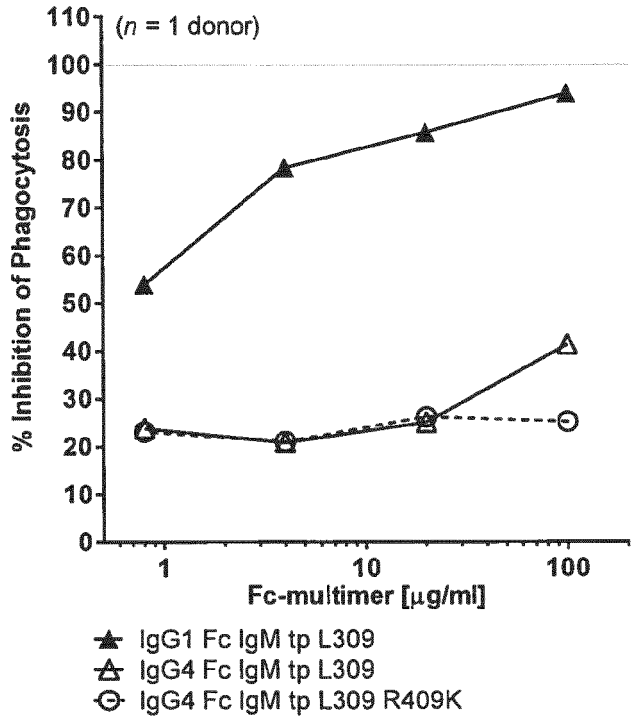
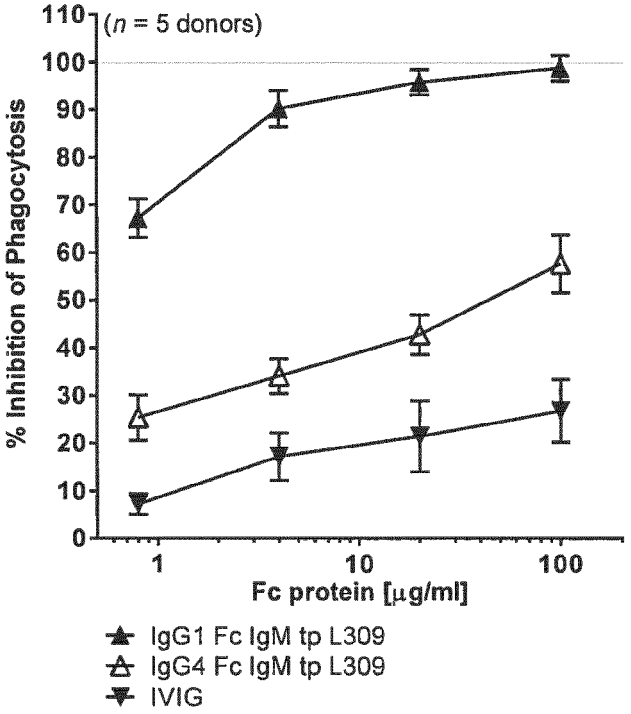


Figure 7


(n = 5 donors)
% Inhibition of Phagocytosis
110
100
90
80
70
60
50
40
30
20
10
0
1
10
100
Fc protein [µg/ml]
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IVIG

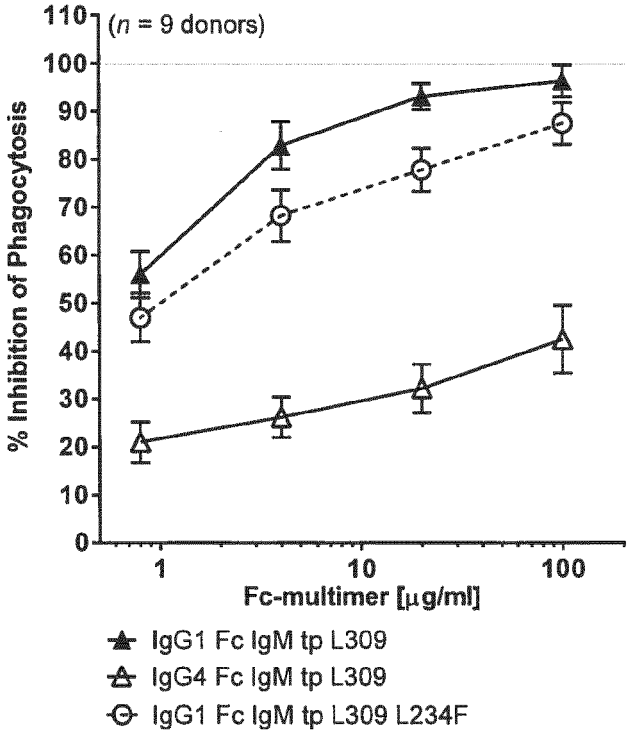
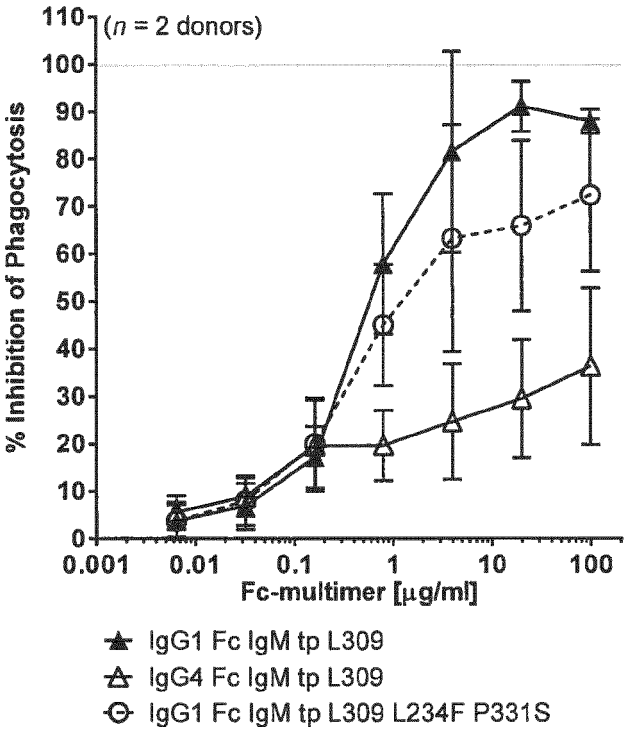

(n = 9 donors)
% Inhibition of Phagocytosis
110
100
90
80
70
60
50
40
30
20
10
0
1
10
100
Fc-multimer [µg/ml]
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309 L234F

Figure 7 continued



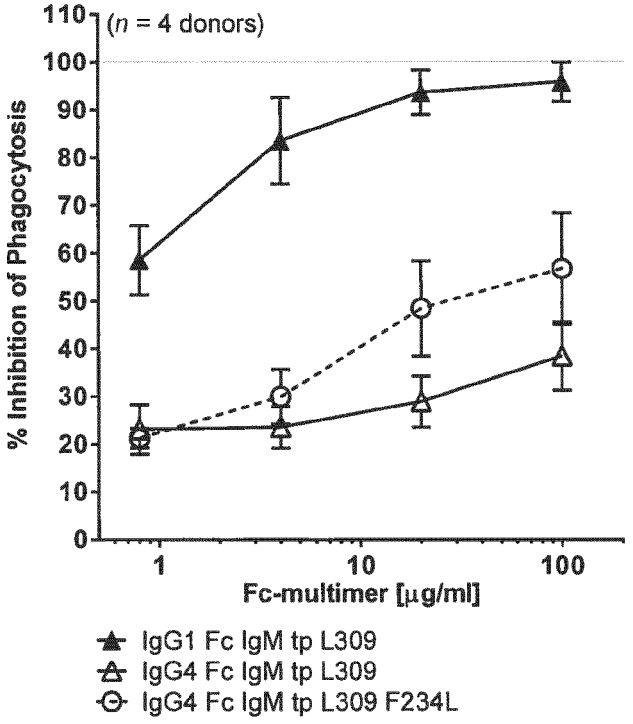
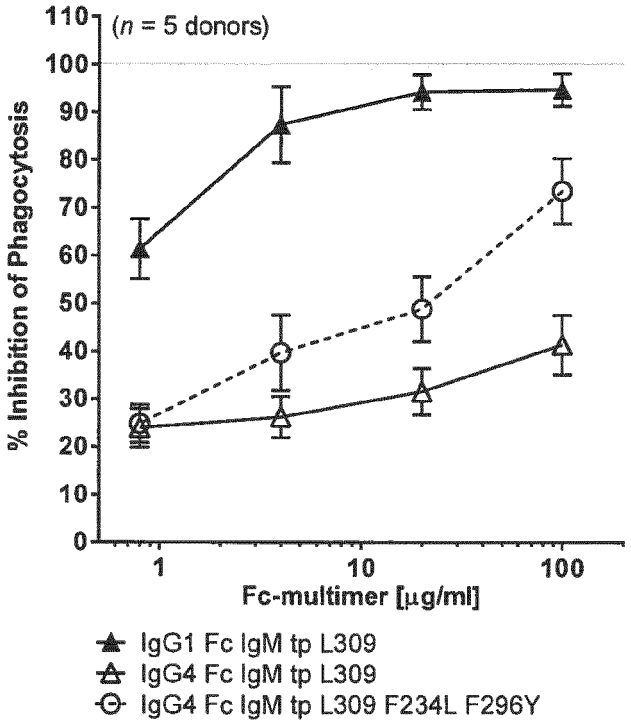


Figure 7 continued



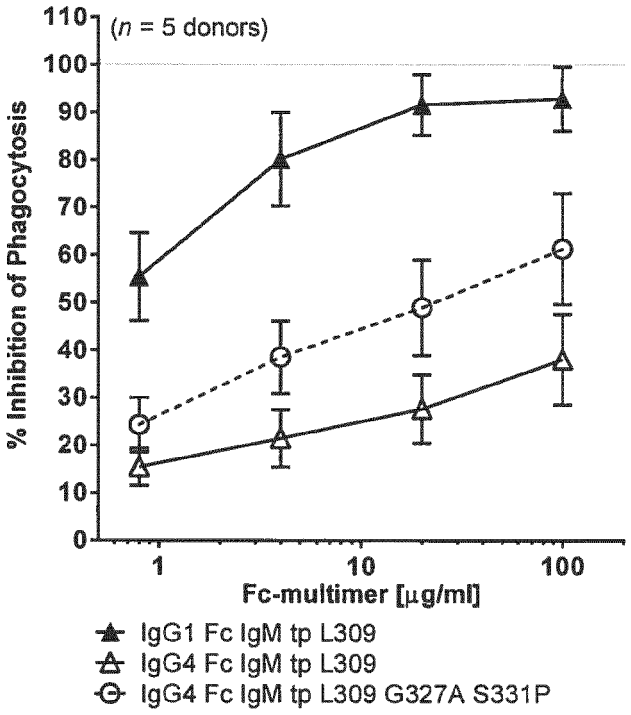
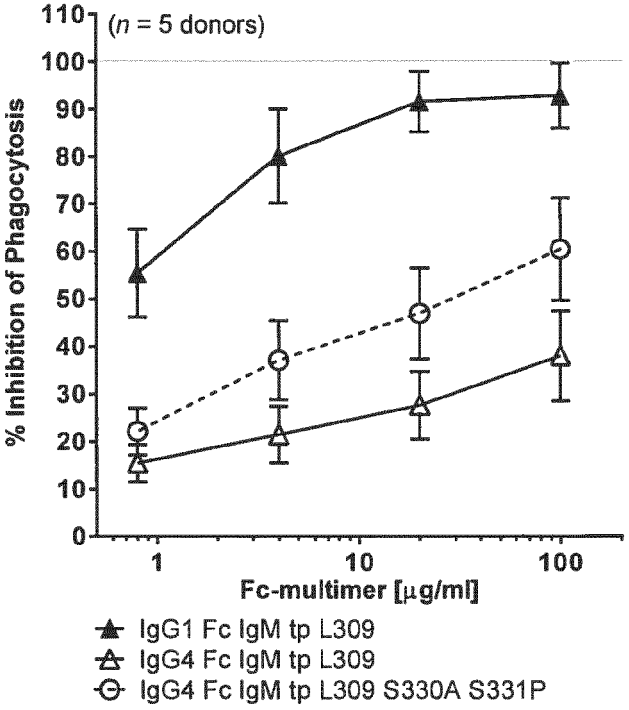


Figure 7 continued



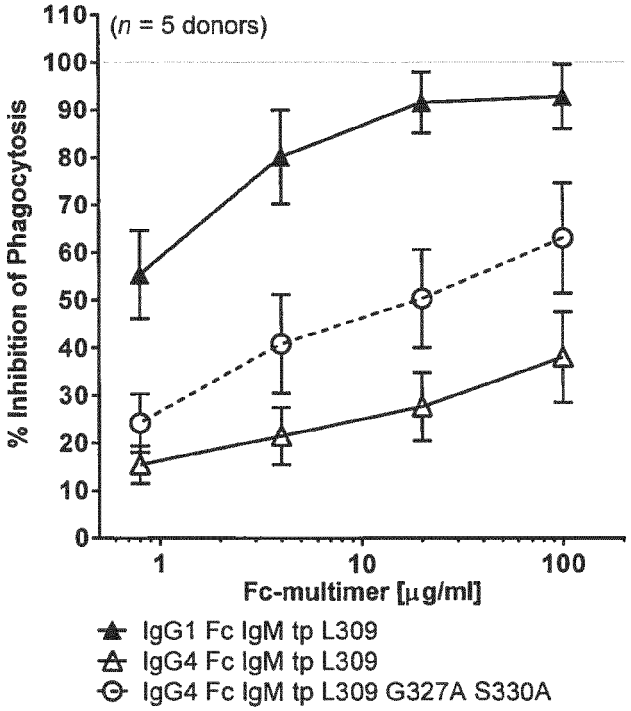


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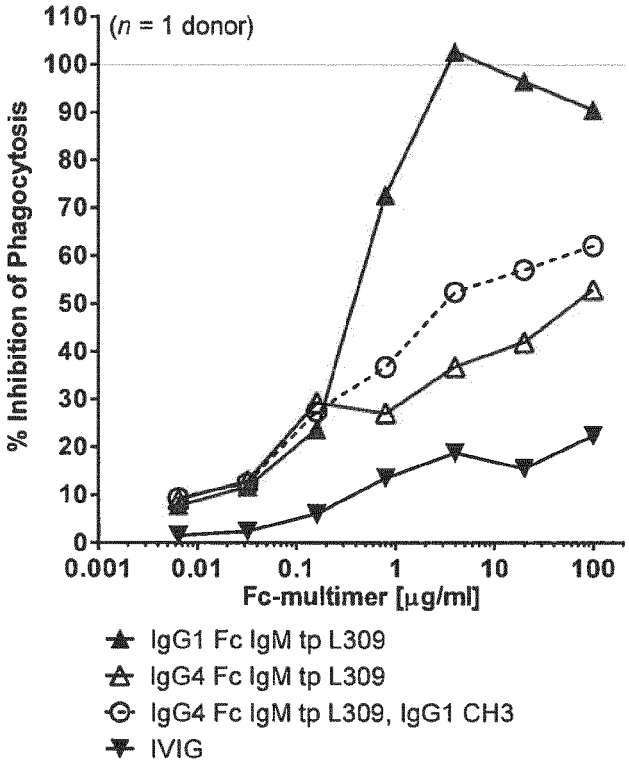


Figure 8

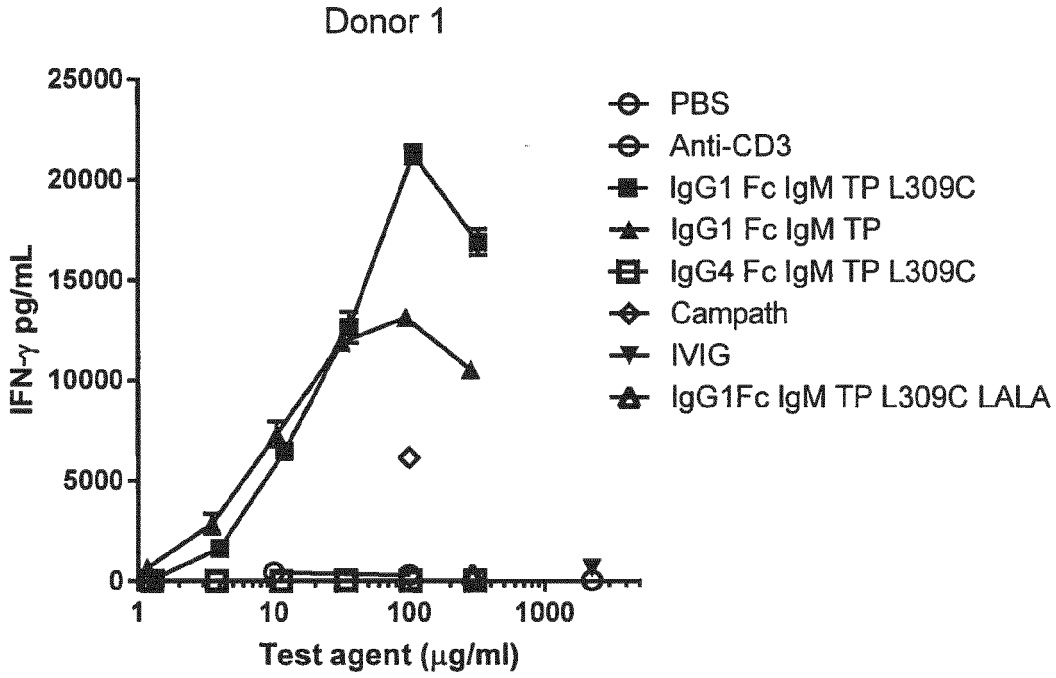
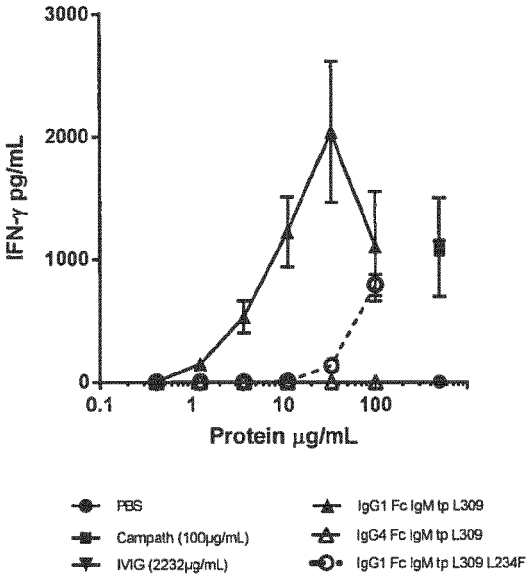

Donor 1
25000
20000
15000
10000
5000
0
IFN-γ pg/mL
1
10
100
1000
Test agent (μg/ml)
PBS
Anti-CD3
IgG1 Fc IgM TP L309C
IgG1 Fc IgM TP
IgG4 Fc IgM TP L309C
Campath
IVIG
IgG1Fc IgM TP L309C LALA

Figure 9


3000
2000
1000
0
IFN-γ pg/mL
0.1
1
10
100
Protein µg/mL
PBS
Campath (100µg/mL)
IVIG (2232µg/mL)
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309 L234F

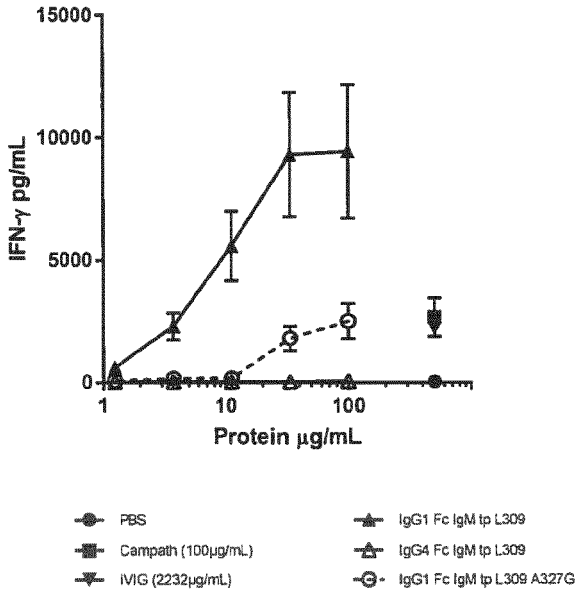
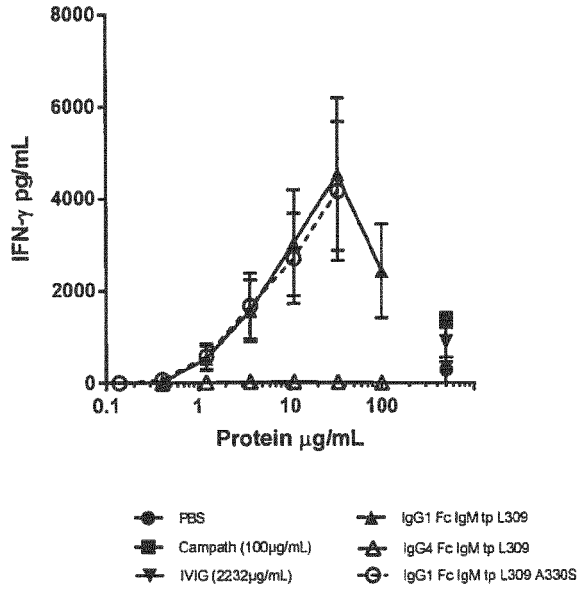

15000
10000
5000
0
IFN-γ pg/mL
1
10
100
Protein µg/mL
PBS
Campath (100µg/mL)
IVIG (2232µg/mL)
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309 A327G

Figure 9 continued



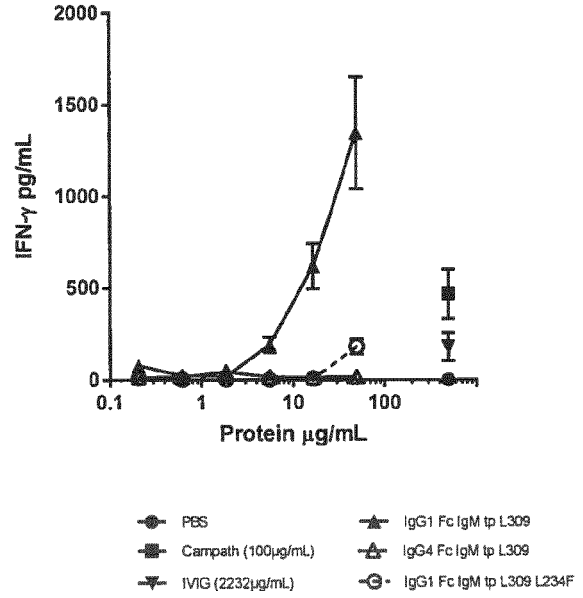
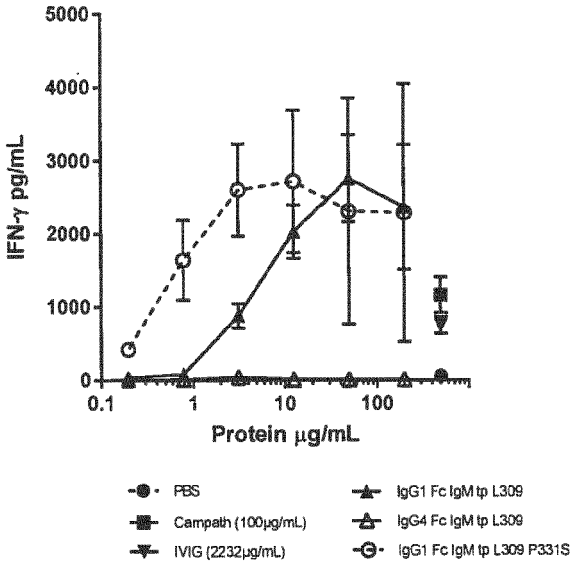


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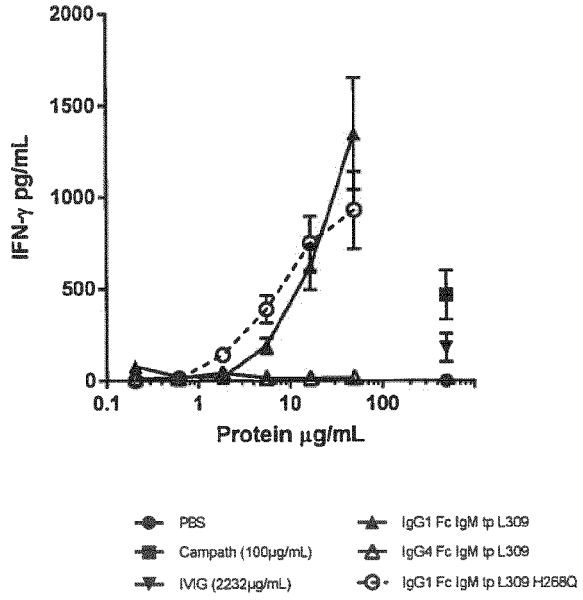
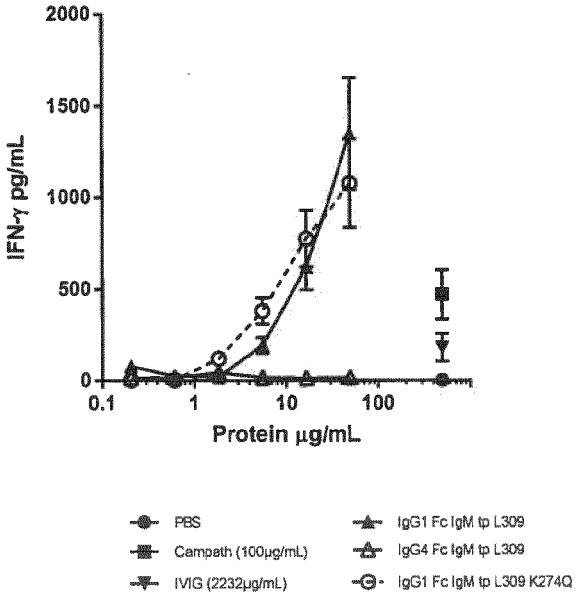


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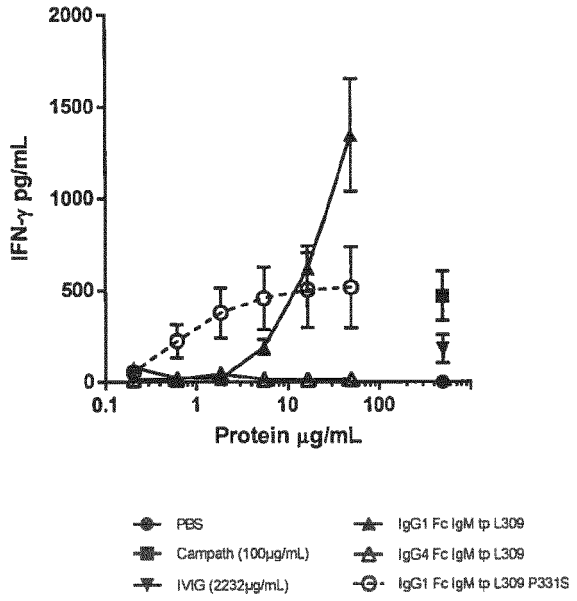
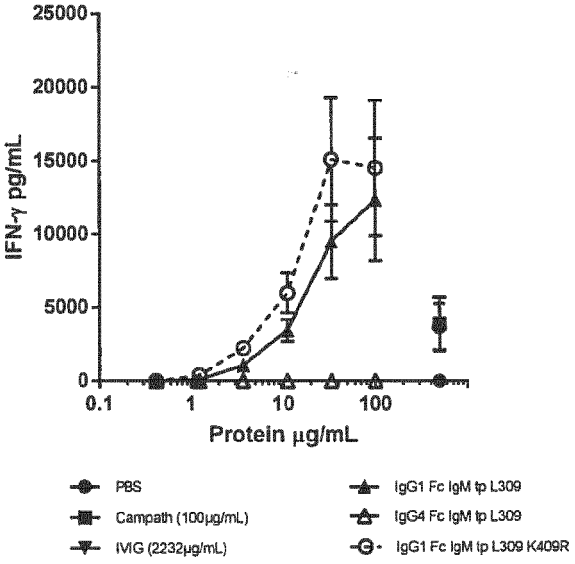


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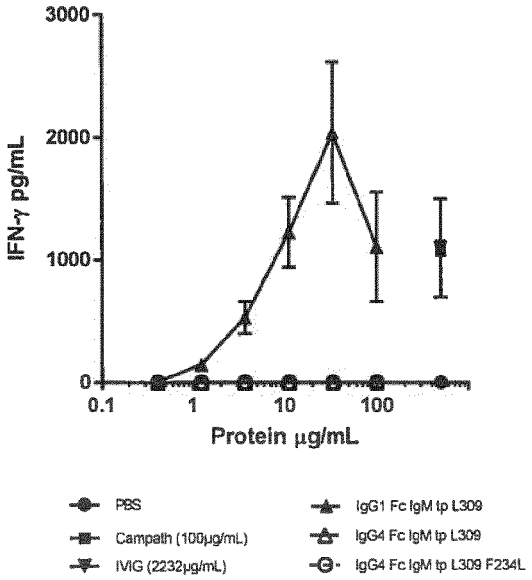
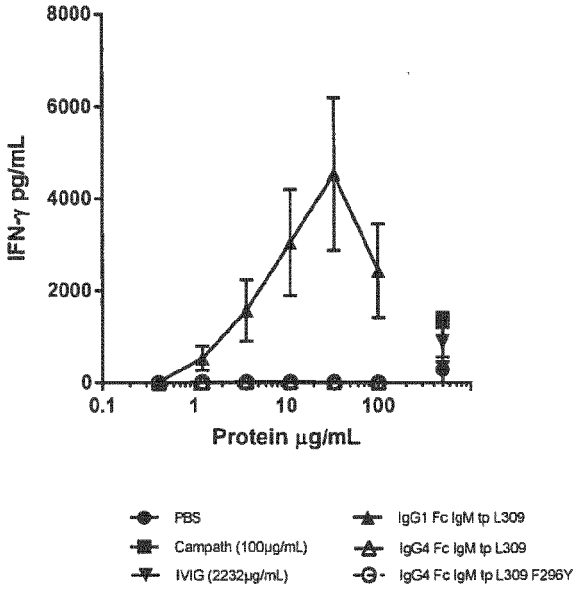


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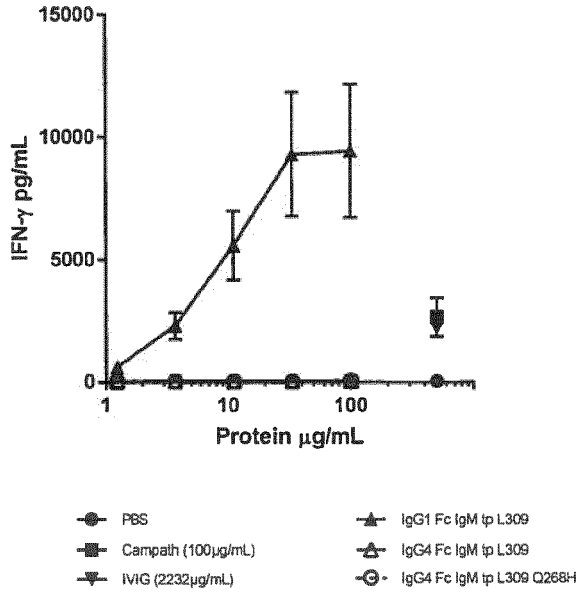
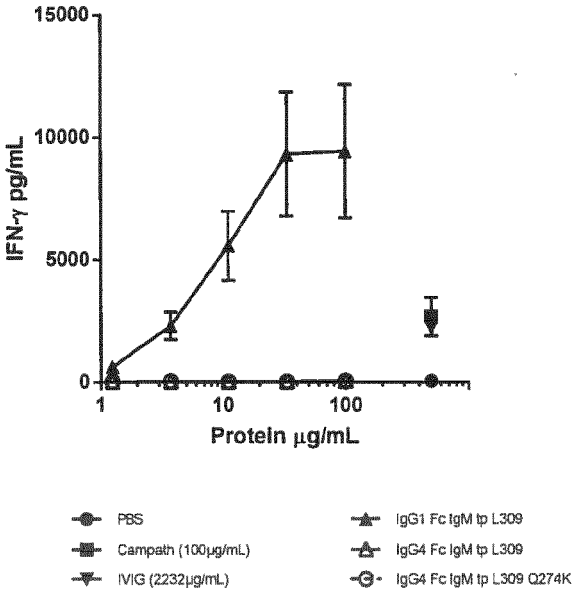


Figure 9 continued



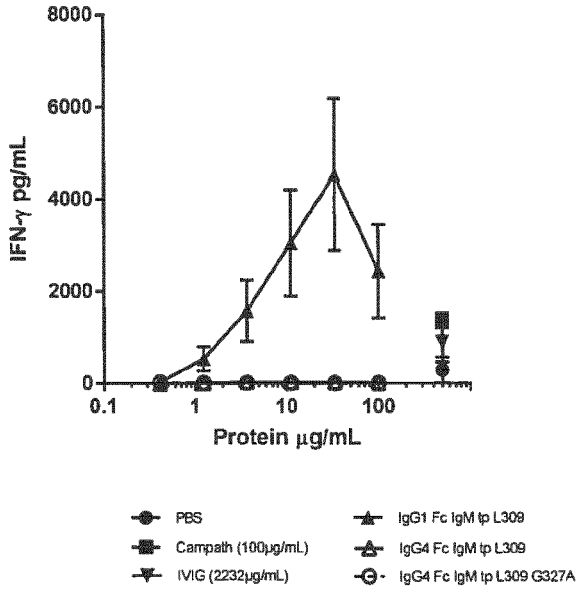
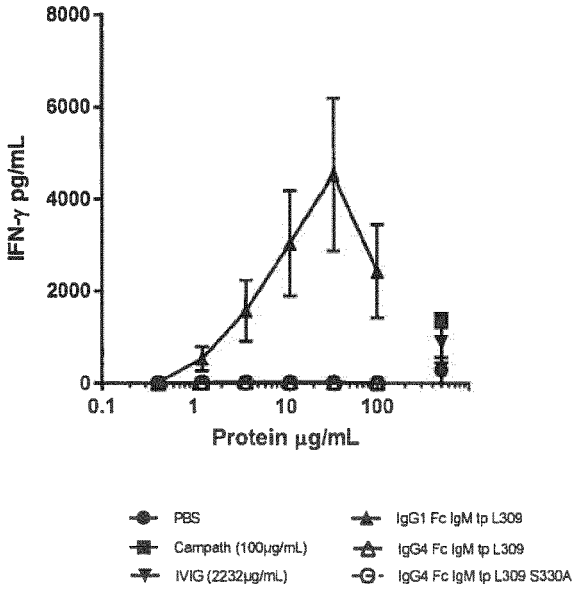


Figure 9 continued



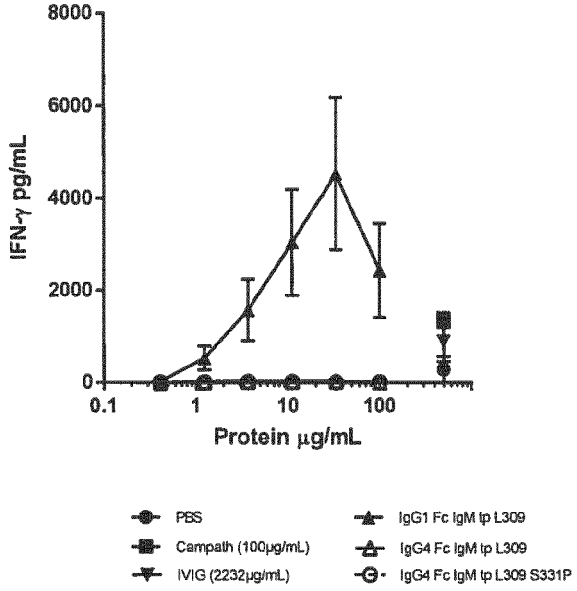


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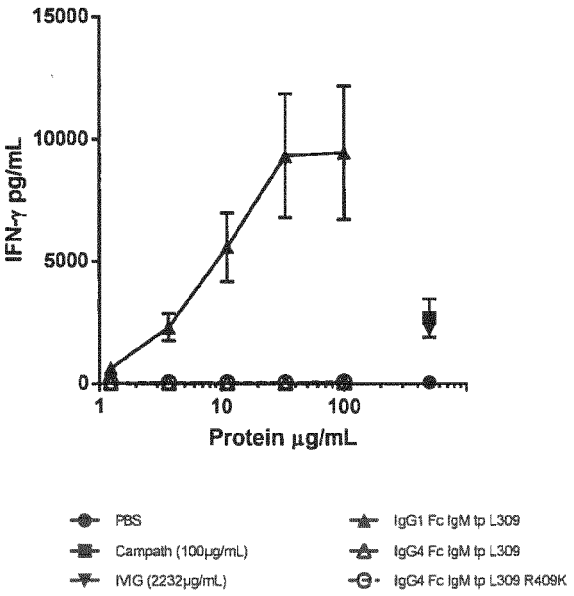
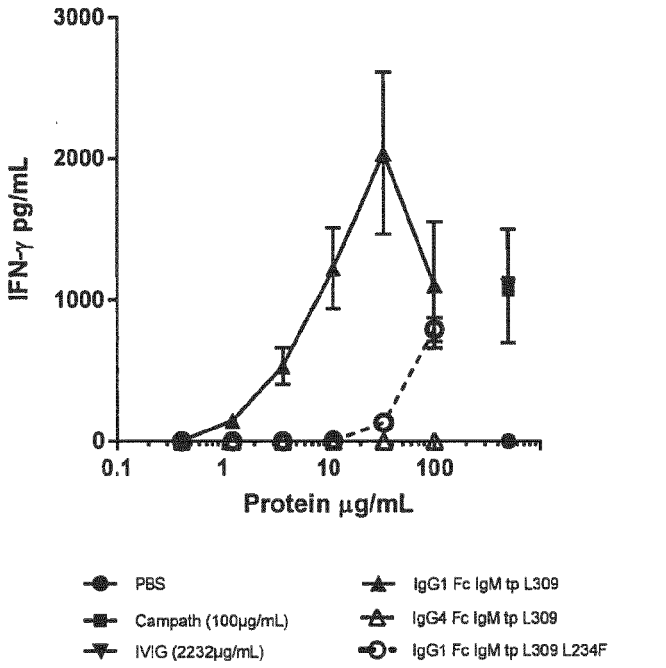


Figure 10


3000
2000
1000
0
IFN-γ pg/mL
0.1
1
10
100
Protein µg/mL
PBS
Campath (100µg/mL)
IVIG (2232µg/mL)
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309 L234F

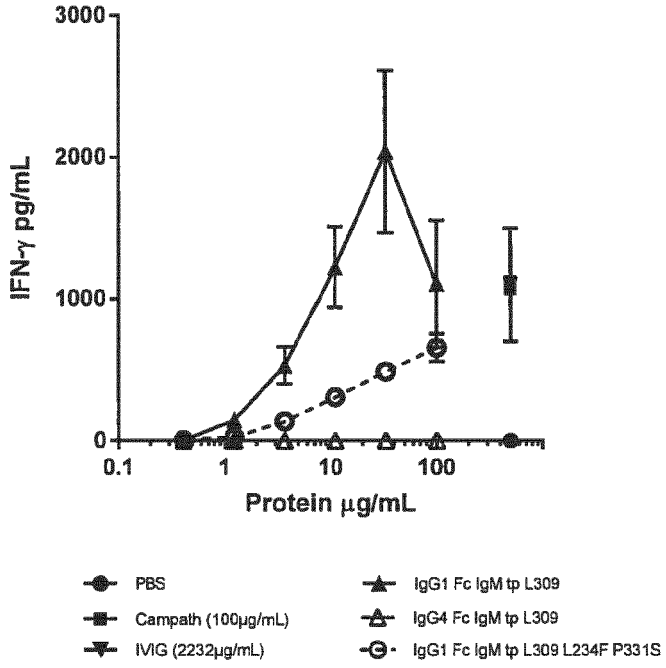
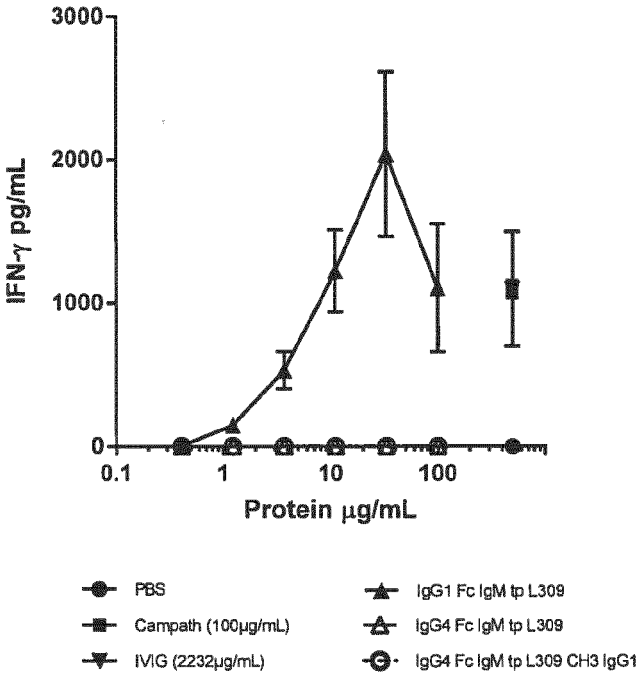

3000
2000
1000
0
IFN-γ pg/mL
0.1
1
10
100
Protein µg/mL
PBS
Campath (100µg/mL)
IVIG (2232µg/mL)
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309 L234F P331S

Figure 10 continued



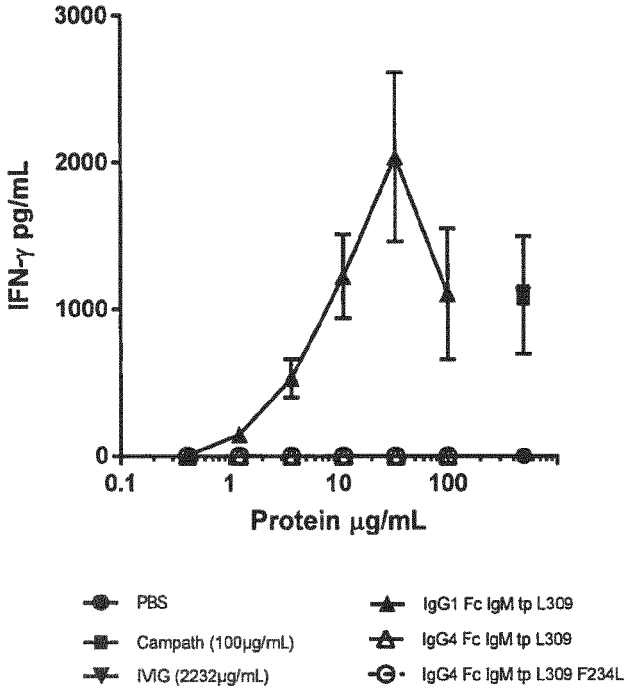
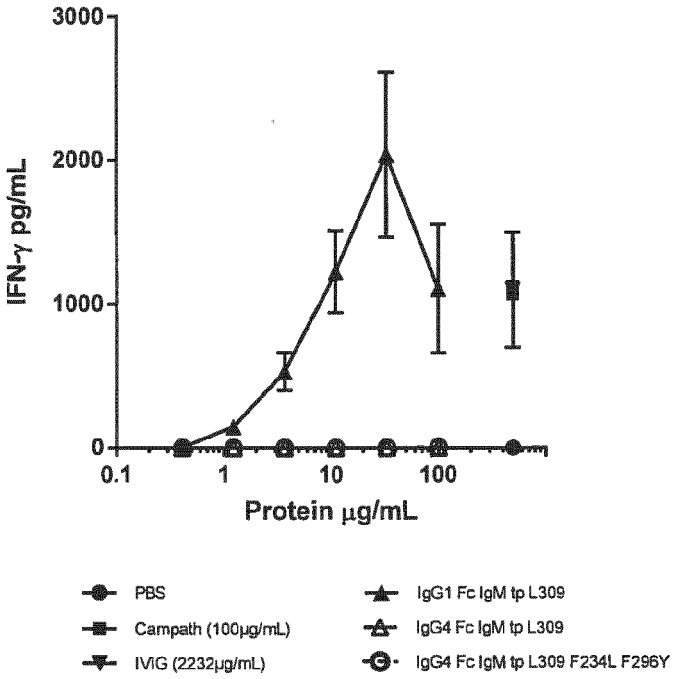


Figure 10 continued



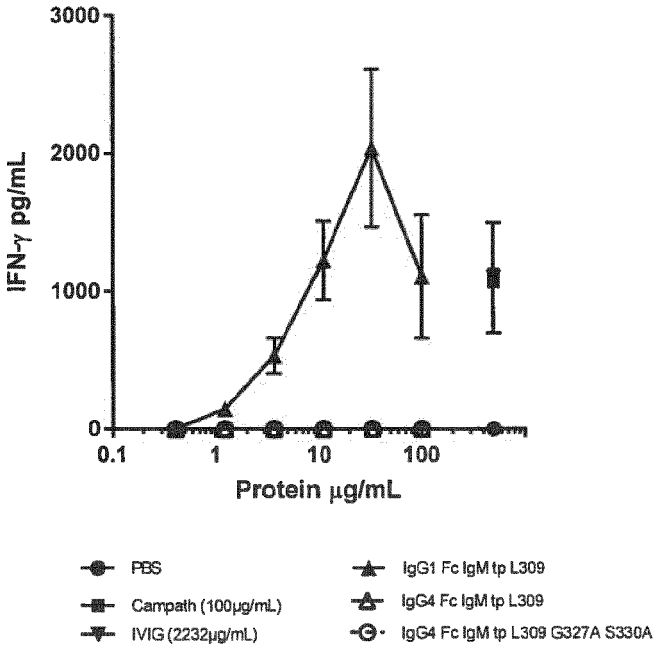
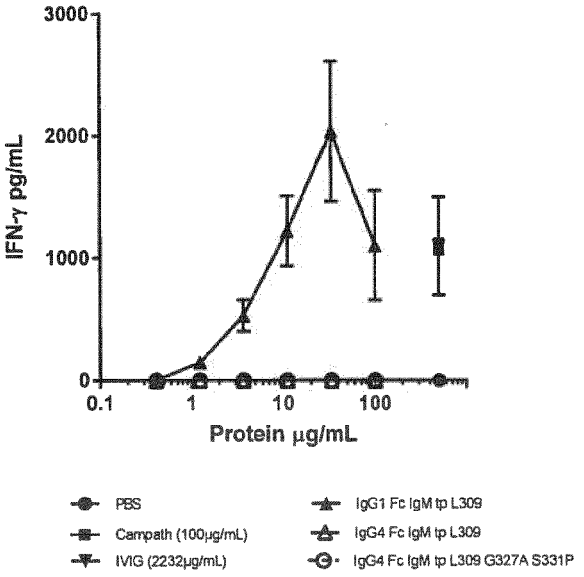


Figure 10 continued



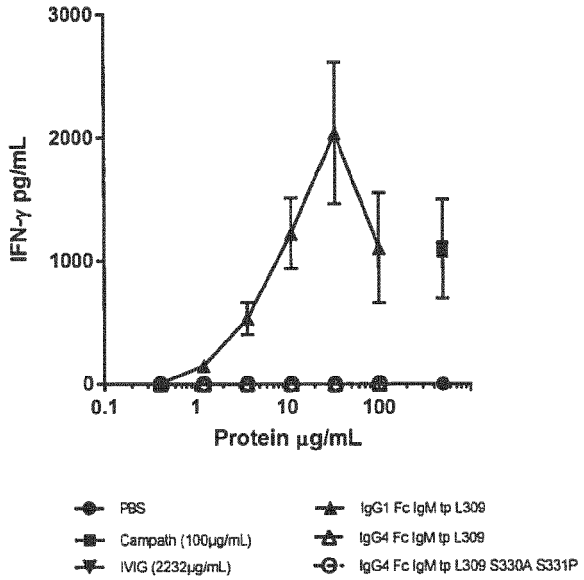
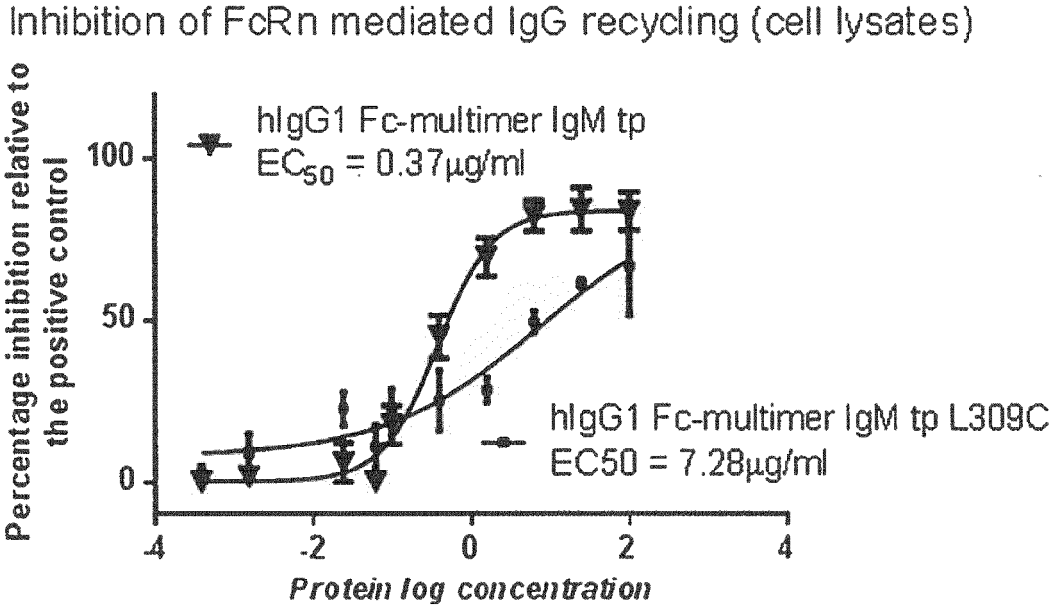


Figure 11


Inhibition of FcRn mediated IgG recycling (cell lysates)
Percentage inhibition relative to the positive control
100
50
0
-4
-2
0
2
4
Protein log concentration
hIgG1 Fc-multimer IgM tp
EC50 = 0.37µg/ml
hIgG1 Fc-multimer IgM tp L309C
EC50 = 7.28µg/ml

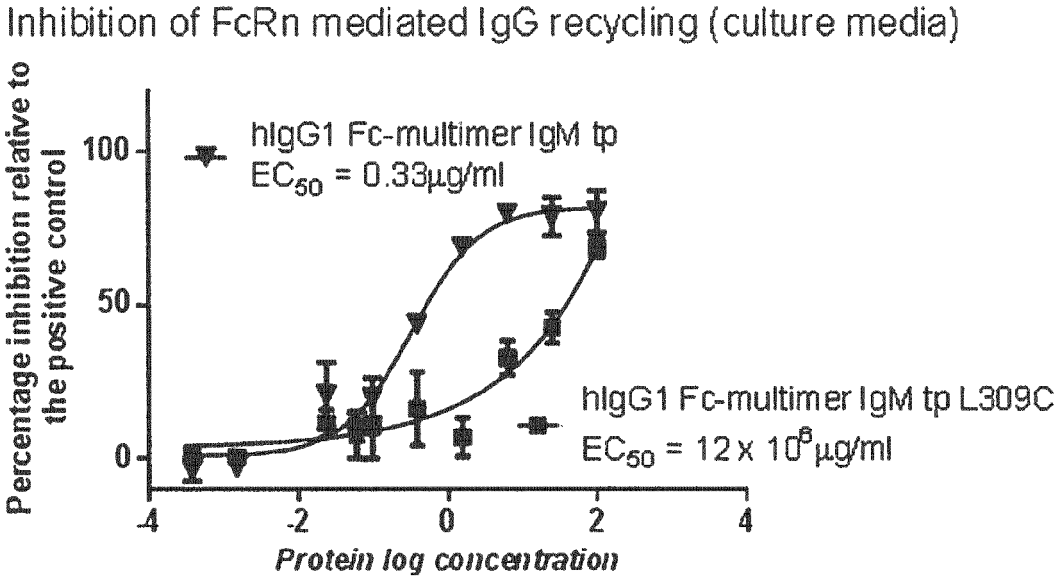

Inhibition of FcRn mediated IgG recycling (culture media)
Percentage inhibition relative to the positive control
100
50
0
-4
-2
0
2
4
Protein log concentration
hIgG1 Fc-multimer IgM tp
EC50 = 0.33µg/ml
hIgG1 Fc-multimer IgM tp L309C
EC50 = 12 x 10^8 µg/ml

Figure 12

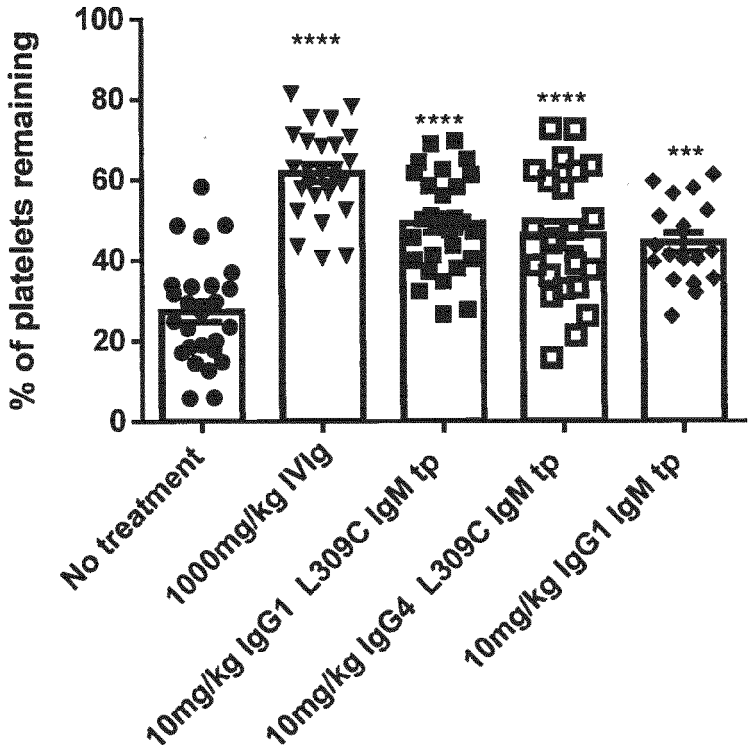
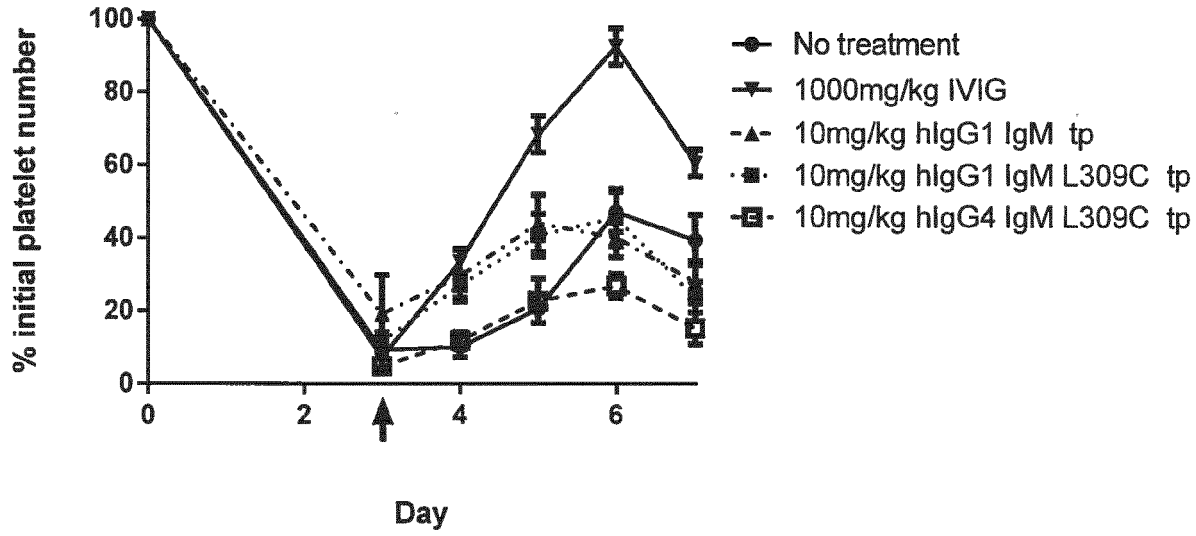

% of platelets remaining
100
80
60
40
20
0
****
****
****
***
No treatment
1000mg/kg IVIg
10mg/kg IgG1 L309C IgM tp
10mg/kg IgG4 L309C IgM tp
10mg/kg IgG1 IgM tp

Figure 13

(a)


% initial platelet number
100
80
60
40
20
0
0
2
4
6
Day
No treatment
1000mg/kg IVIG
10mg/kg hIgG1 IgM tp
10mg/kg hIgG1 IgM L309C tp
10mg/kg hIgG4 IgM L309C tp

(b)

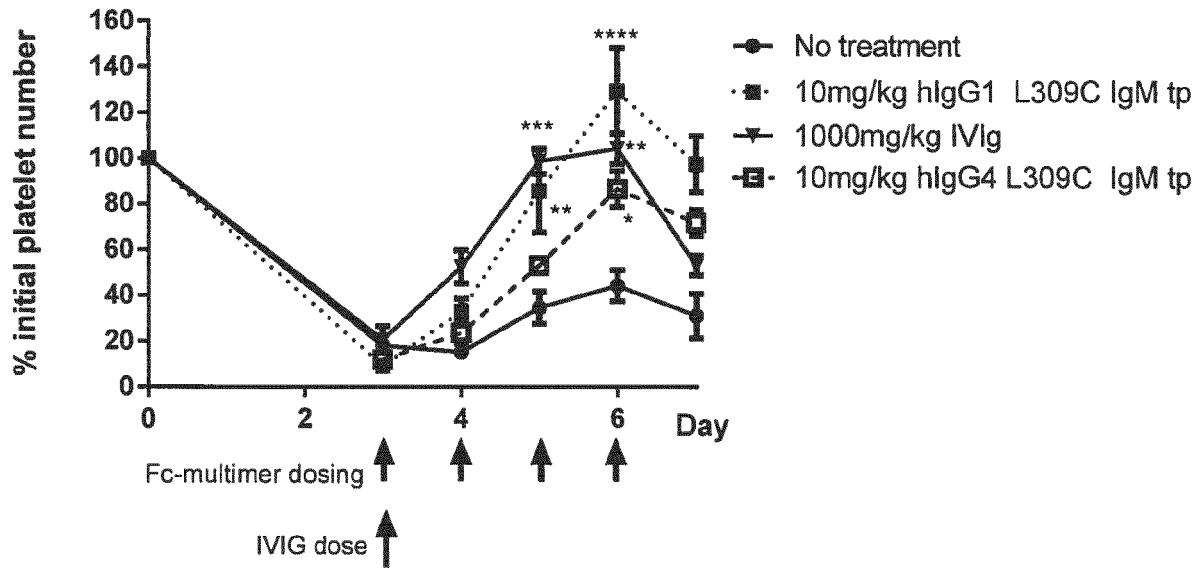
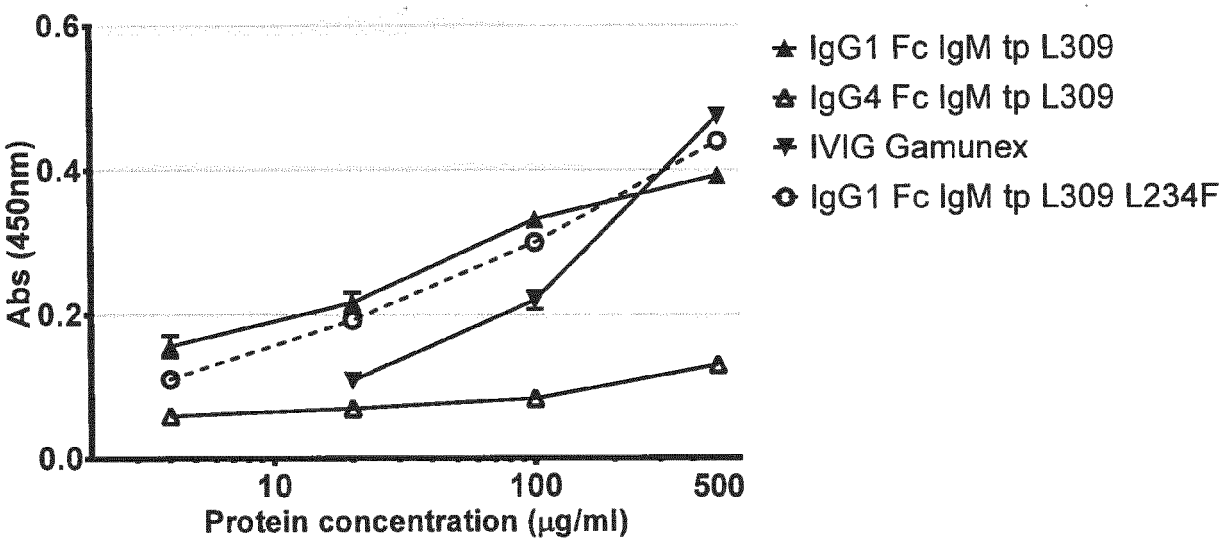

% initial platelet number
160
140
120
100
80
60
40
20
0
0
2
4
6
Day
****
***
**
**
*
Fc-multimer dosing
IVIG dose
No treatment
10mg/kg hIgG1 L309C IgM tp
1000mg/kg IVIg
10mg/kg hIgG4 L309C IgM tp

Figure 14


0.6
0.4
0.2
0.0
Abs (450nm)
10
100
500
Protein concentration (µg/ml)
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IVIG Gamunex
IgG1 Fc IgM tp L309 L234F

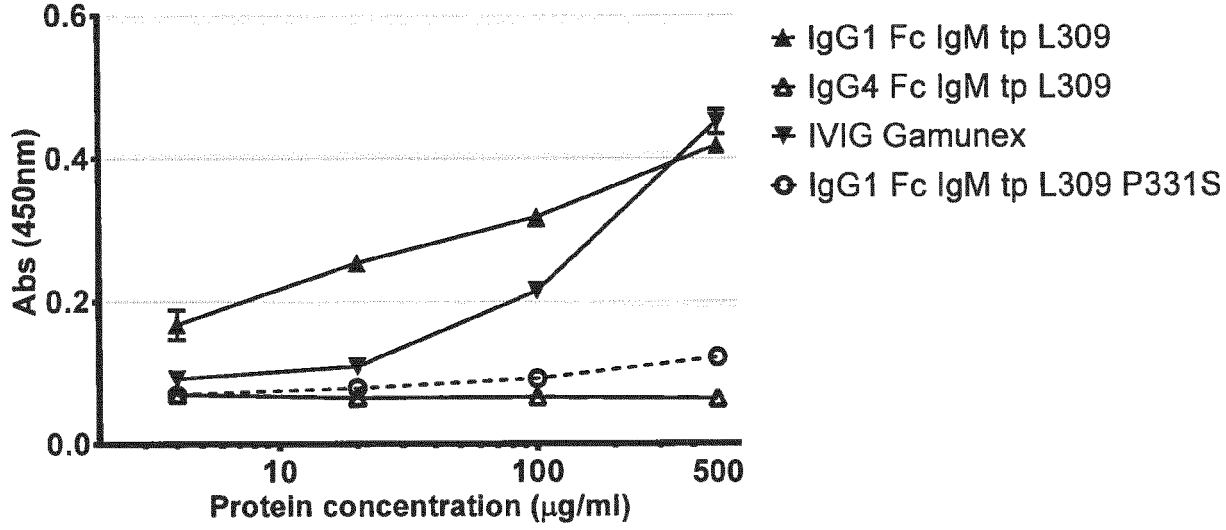
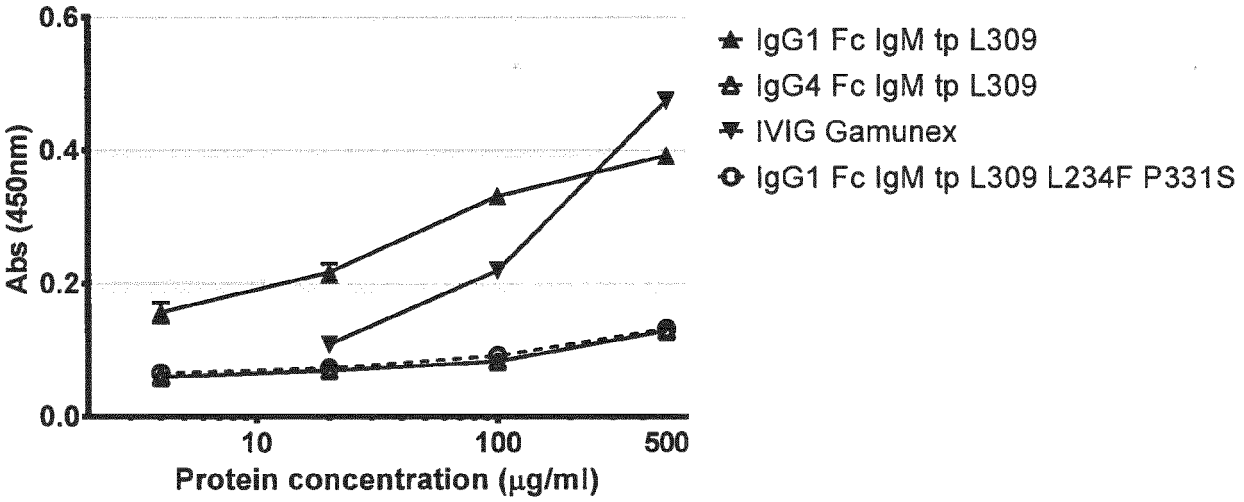

0.6
0.4
0.2
0.0
Abs (450nm)
10
100
500
Protein concentration (µg/ml)
IgG1 Fc IgM tp L309
IgG4 Fc IgM tp L309
IVIG Gamunex
IgG1 Fc IgM tp L309 P331S

Figure 14 continued



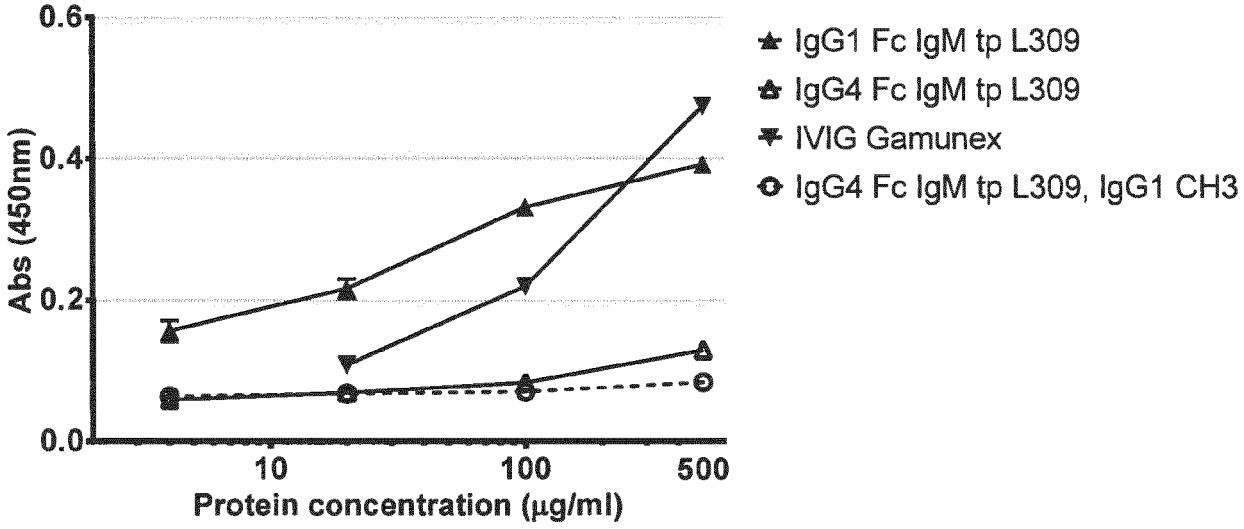
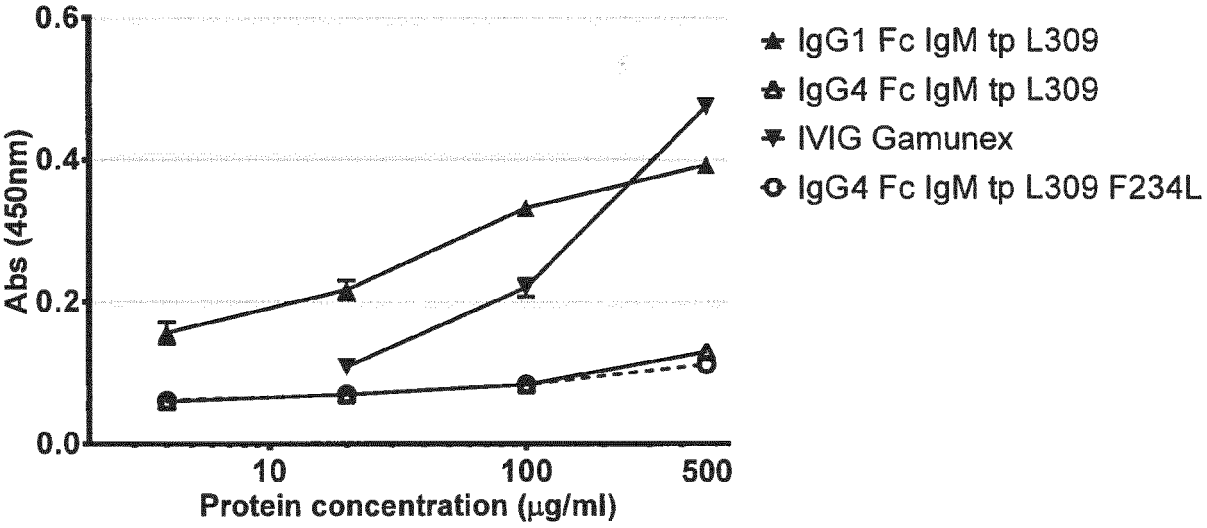


Figure 14 continued



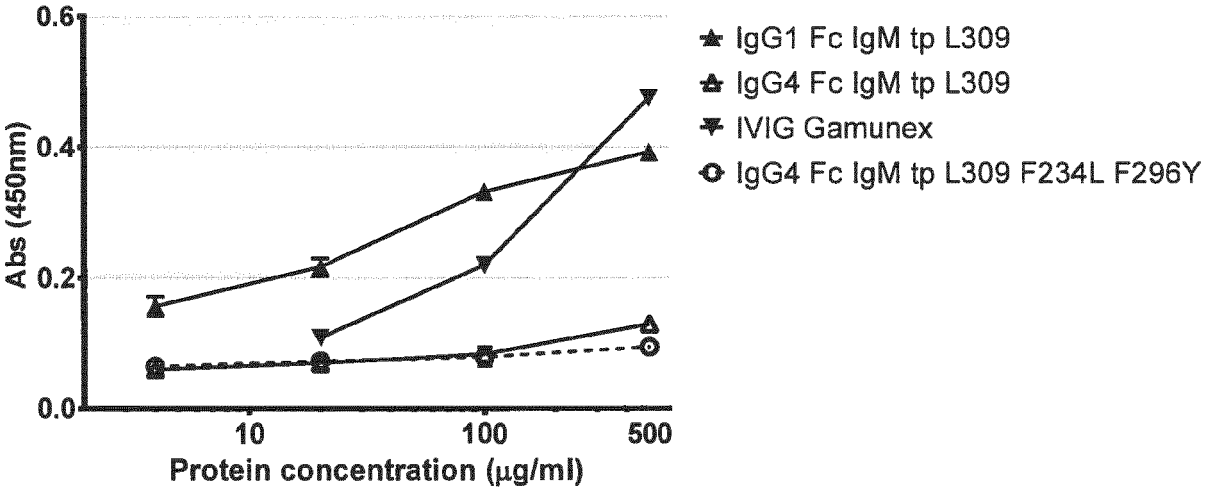
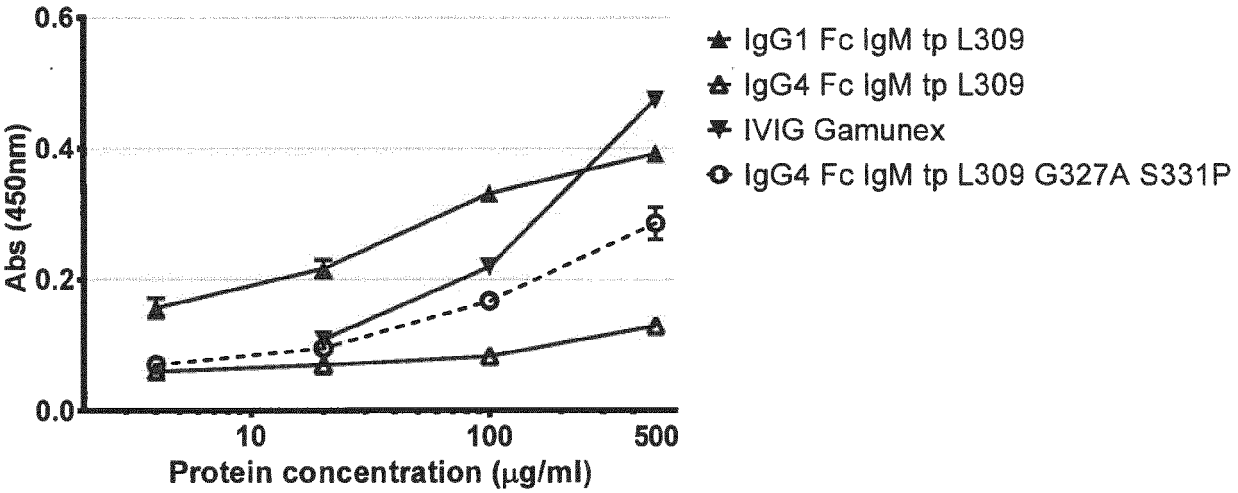


Figure 14 continued



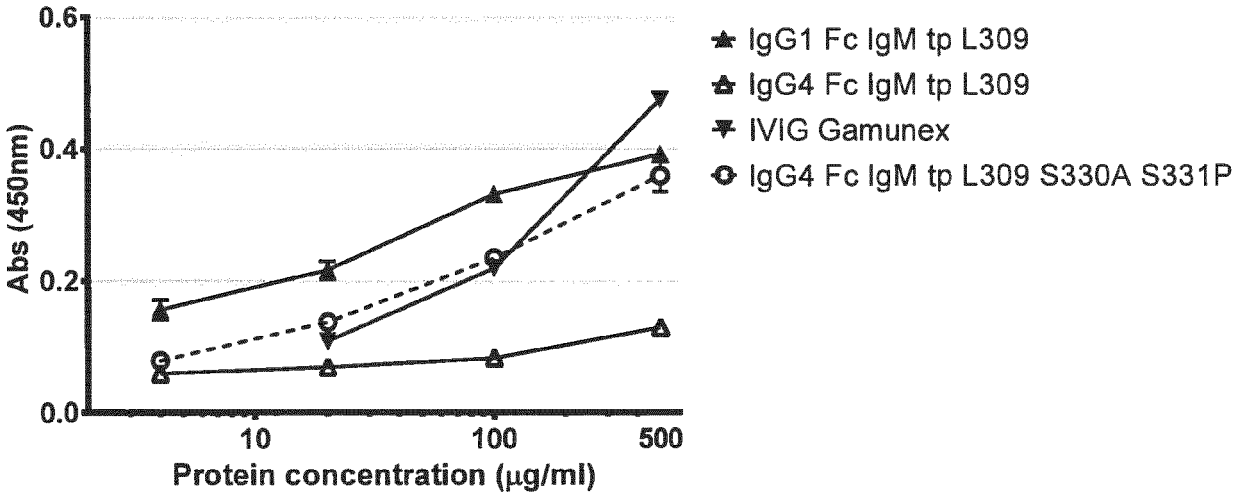


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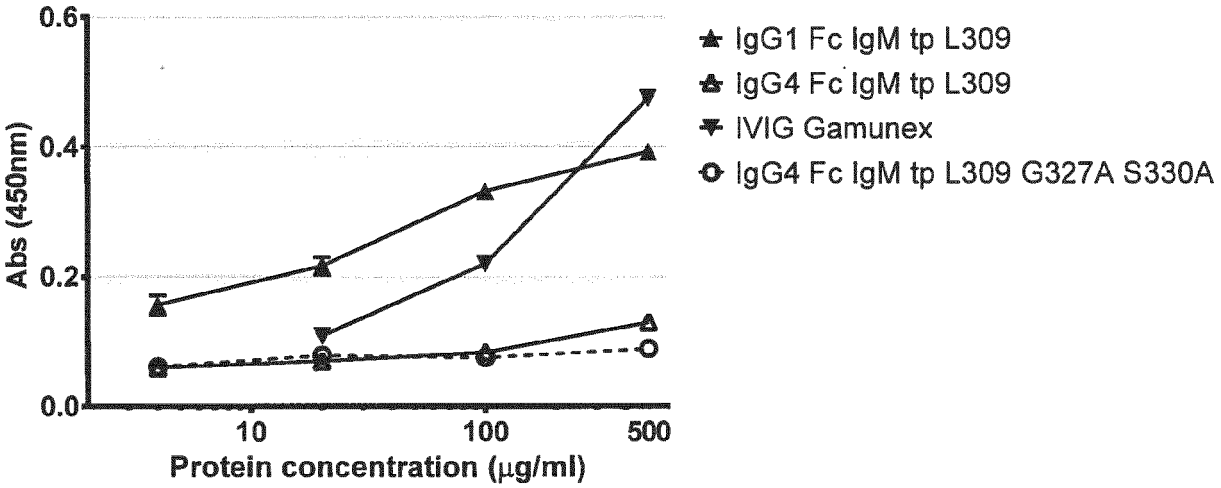


Figure 15

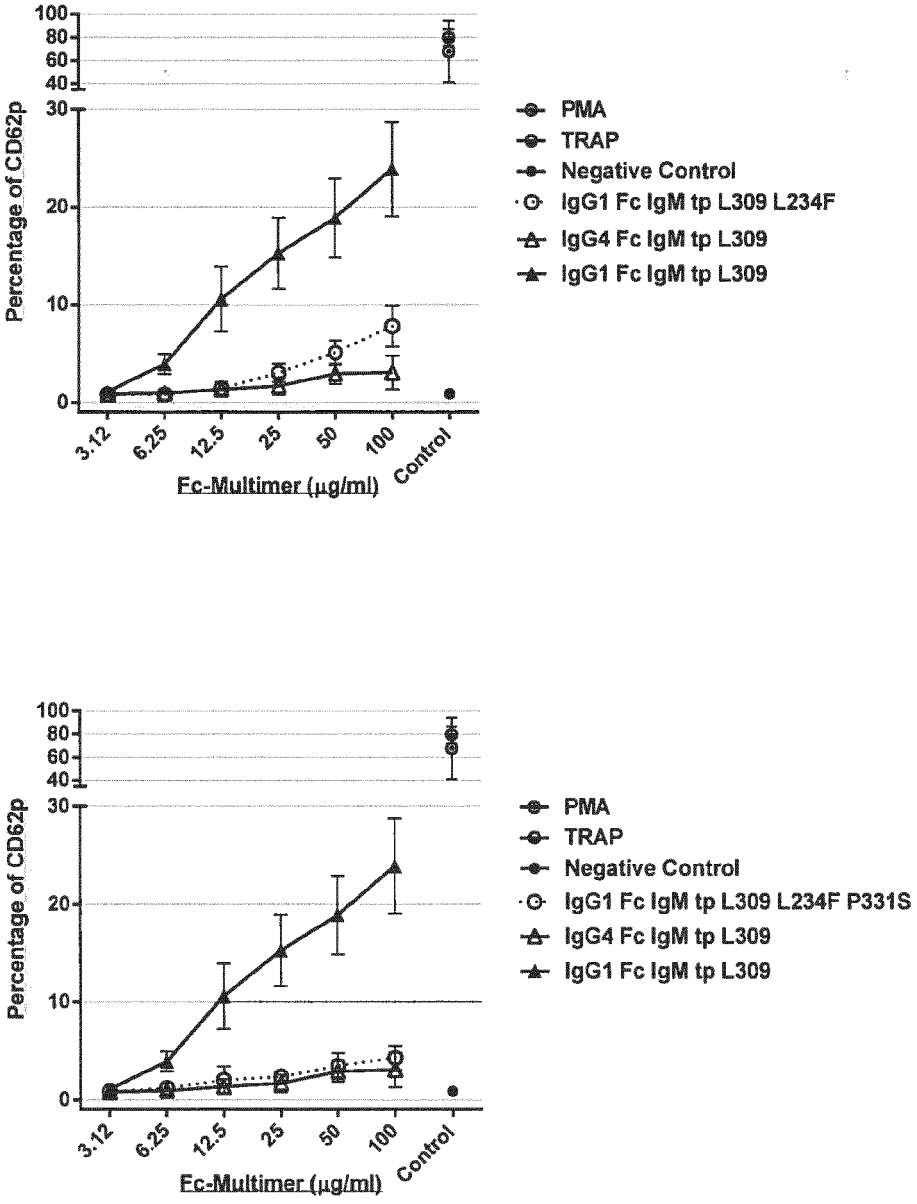
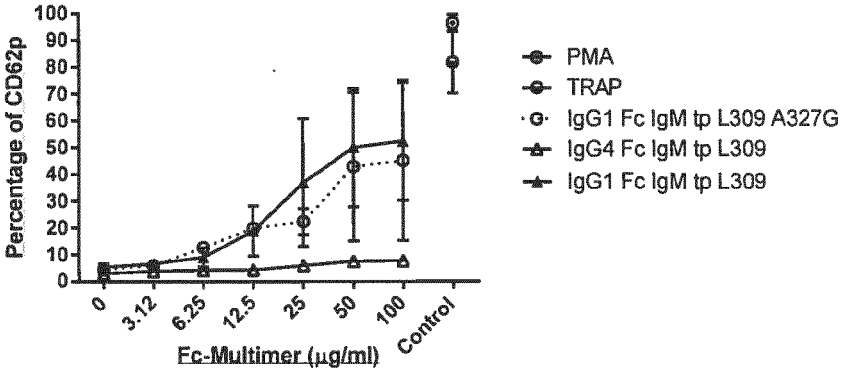

Percentage of CD62p
100
80
60
40
30
20
10
0
3.12
6.25
12.5
25
50
100
Control
Fc-Multimer (µg/ml)
PMA
TRAP
Negative Control
IgG1 Fc IgM tp L309 L234F
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309
Percentage of CD62p
100
80
60
40
30
20
10
0
3.12
6.25
12.5
25
50
100
Control
Fc-Multimer (µg/ml)
PMA
TRAP
Negative Control
IgG1 Fc IgM tp L309 L234F P331S
IgG4 Fc IgM tp L309
IgG1 Fc IgM tp L309

Figure 15 continued



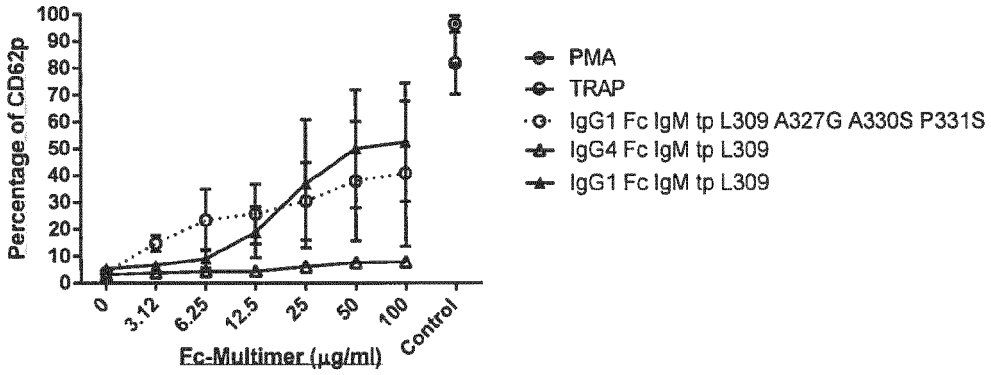
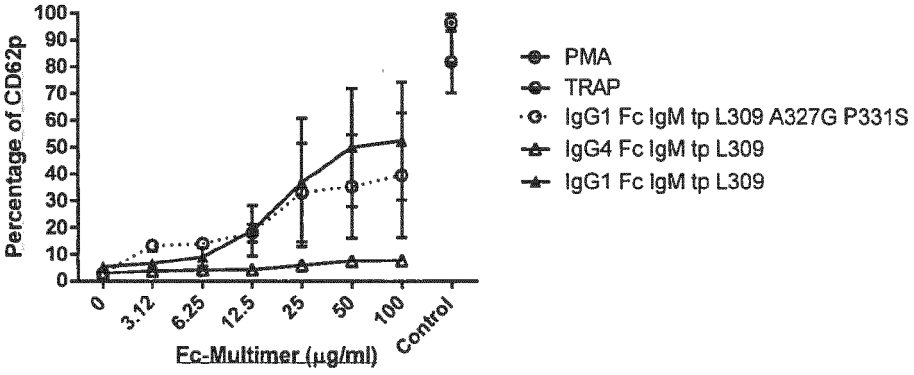


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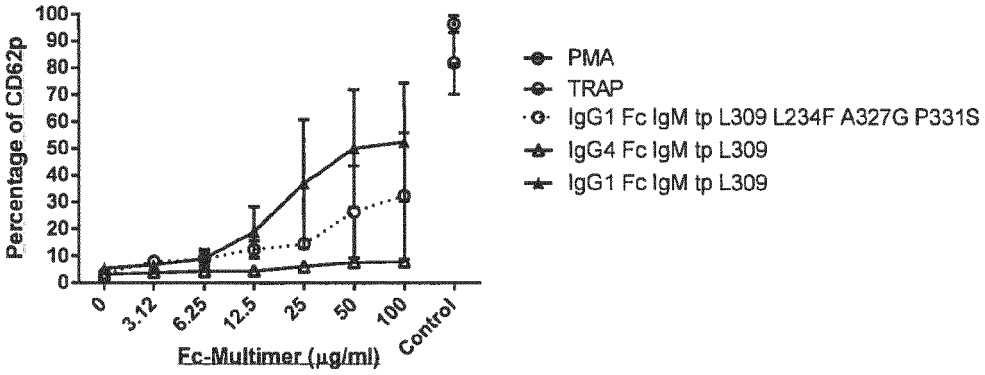
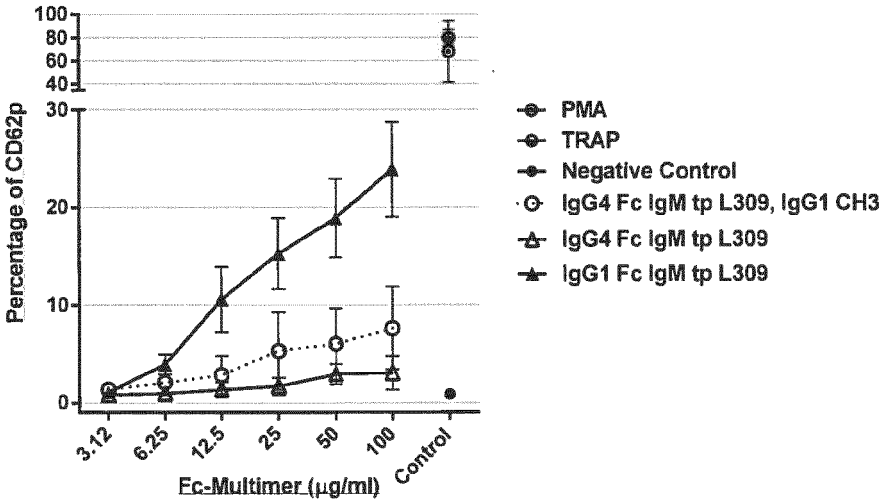


Figure 15 continued



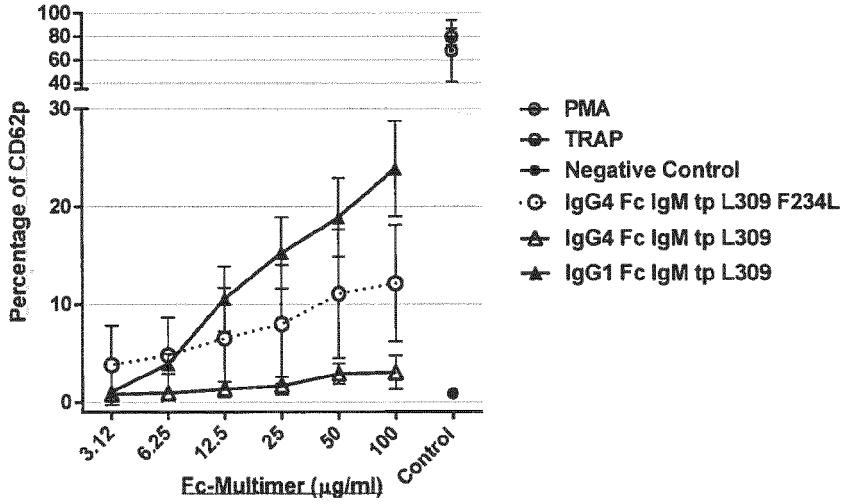
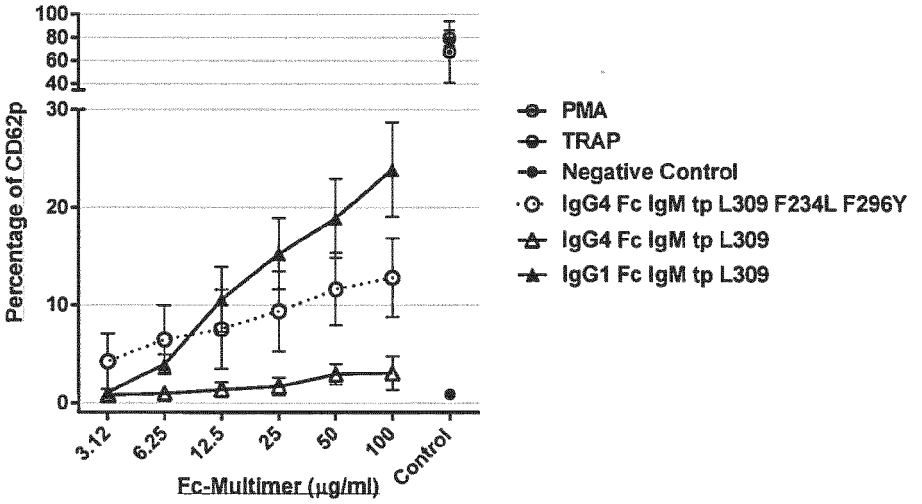


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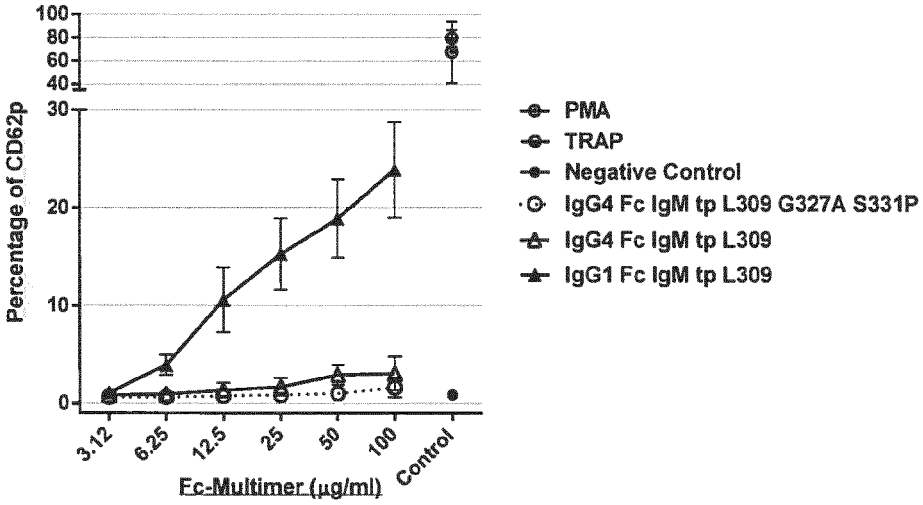


Figure 15 continued

