

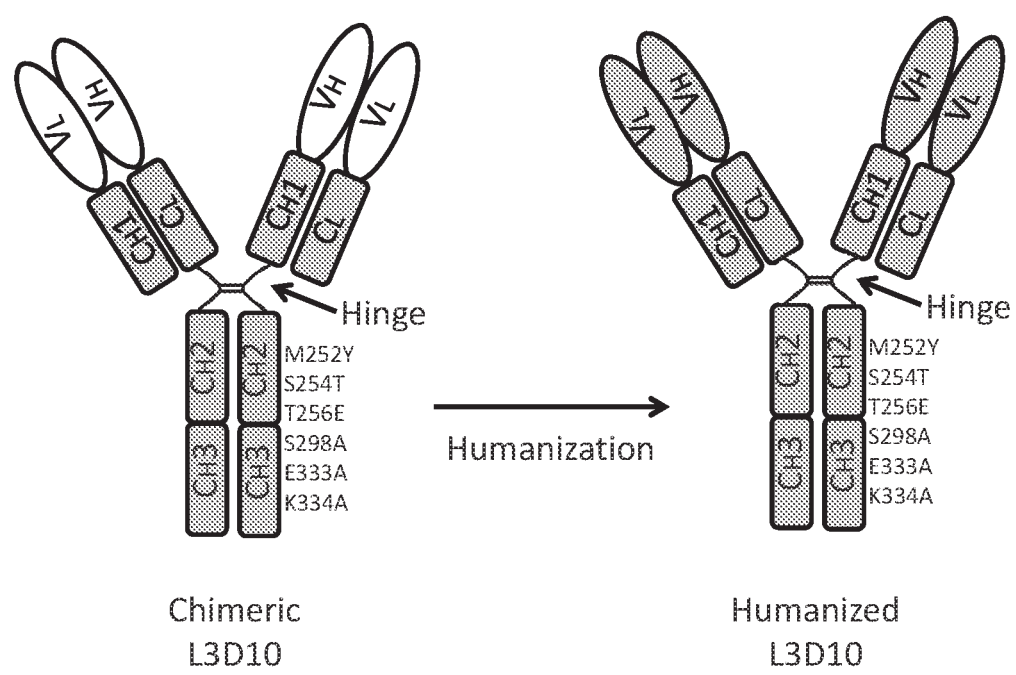


FIG. 1

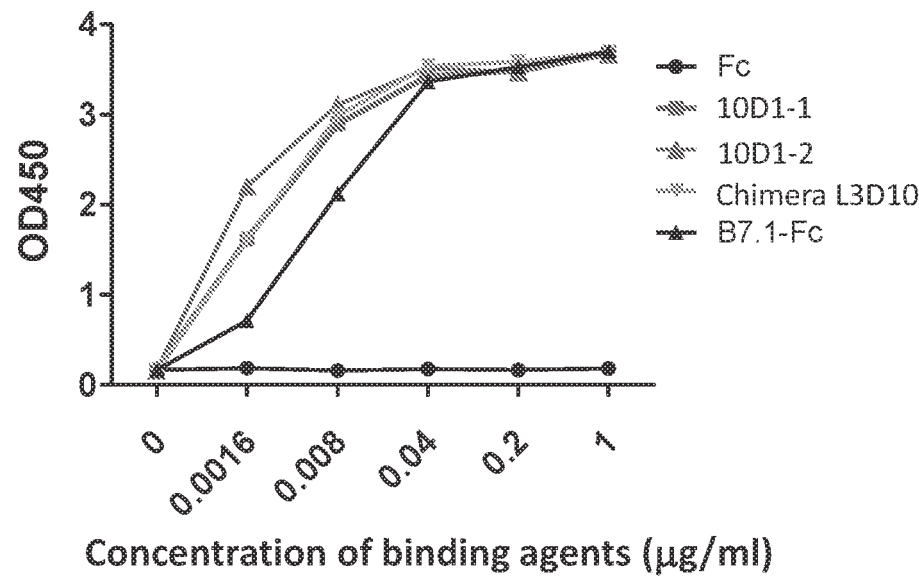


FIG. 2

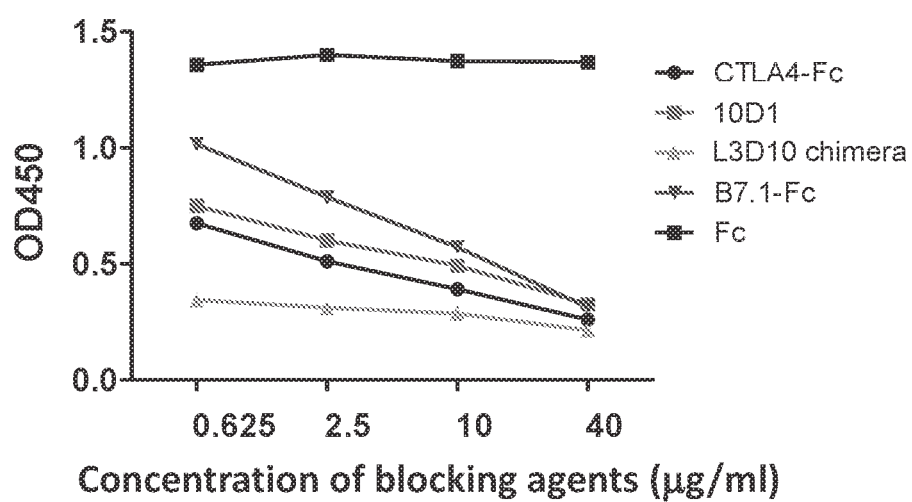


FIG. 3

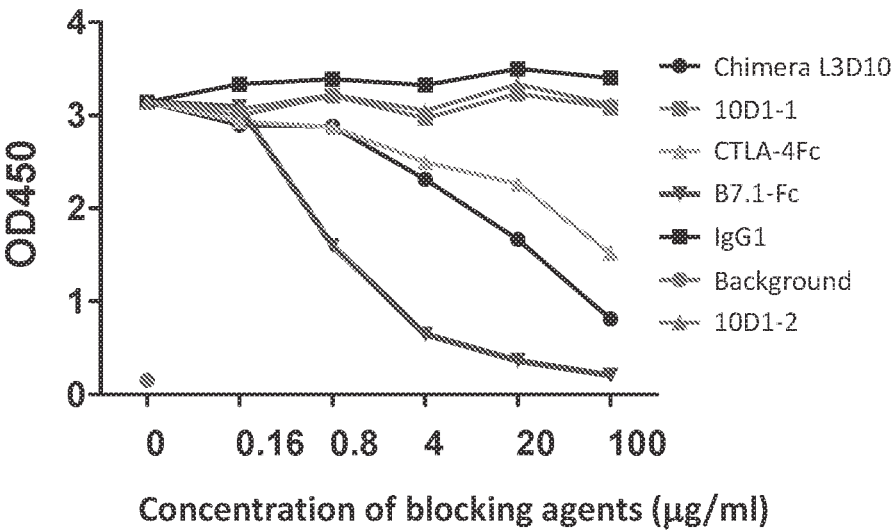


FIG. 4

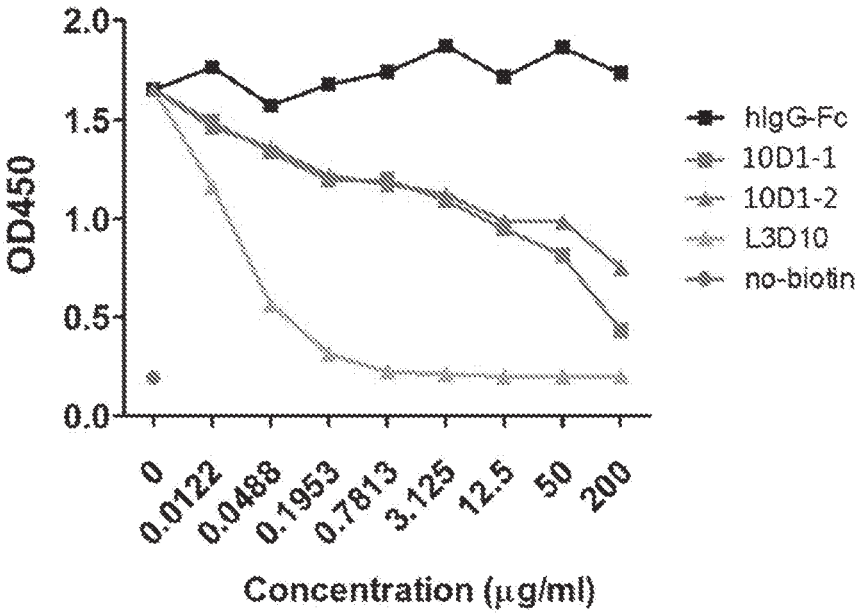


FIG. 5

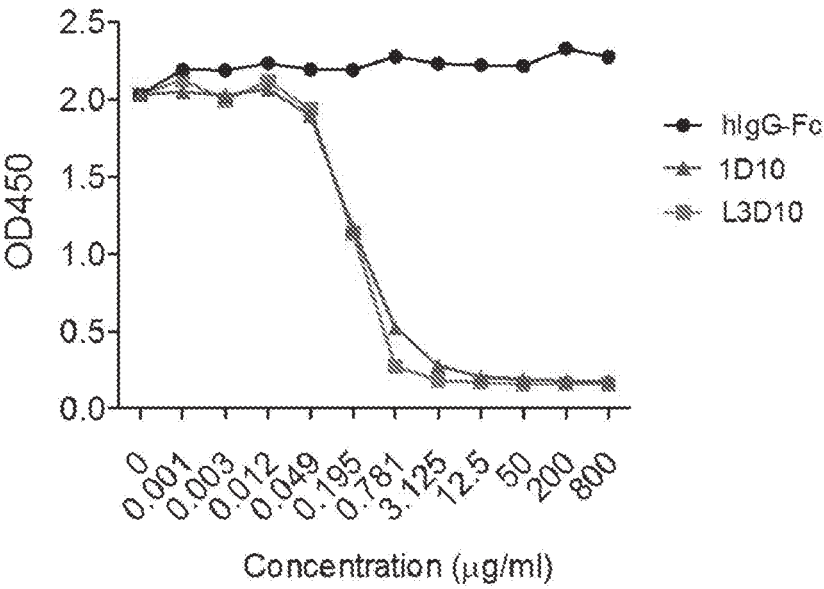


FIG. 6

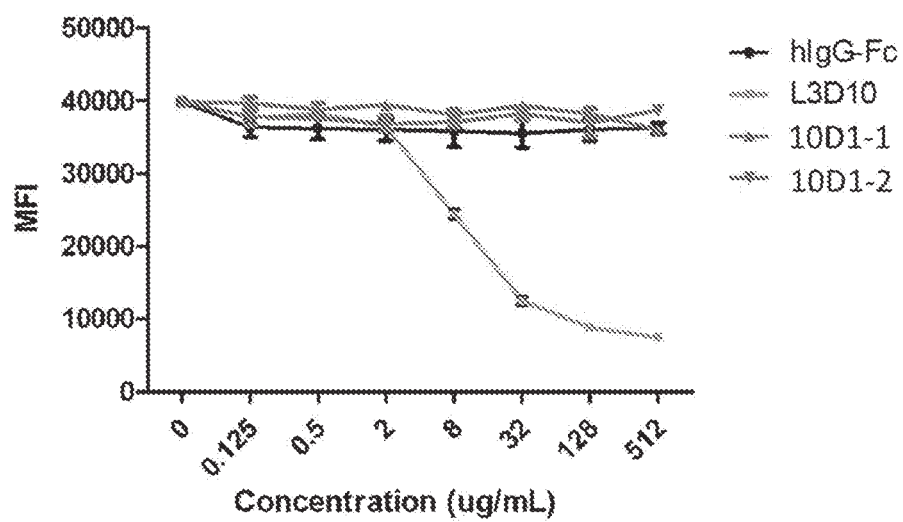


FIG. 7

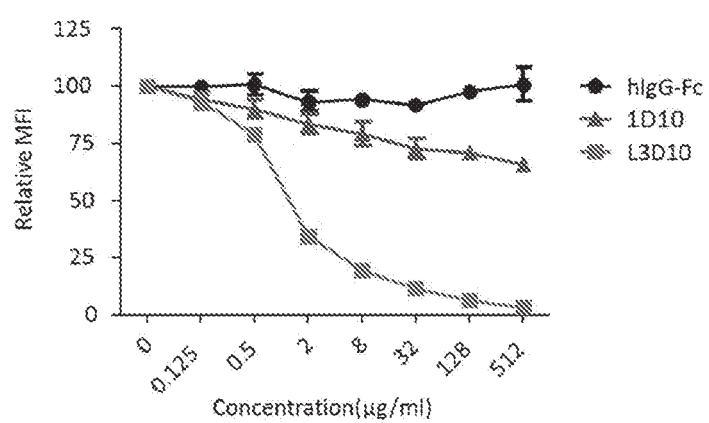


FIG. 8

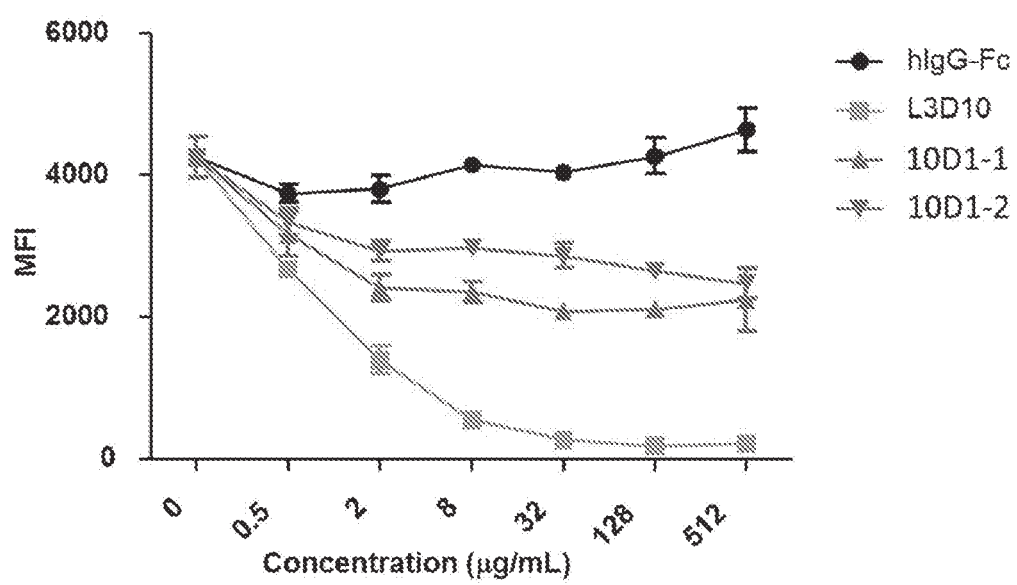


FIG. 9

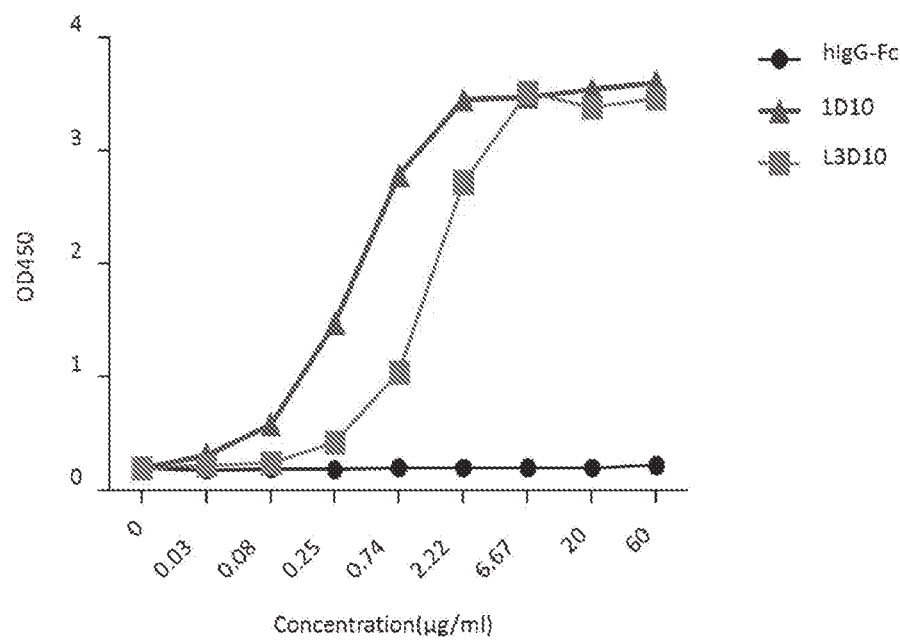


FIG. 10

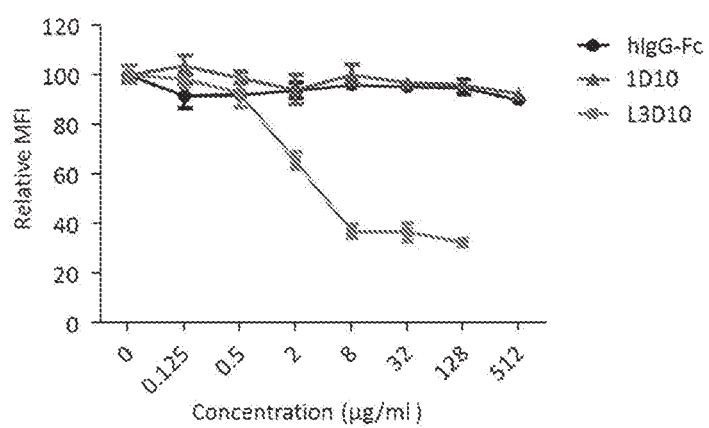


FIG. 11

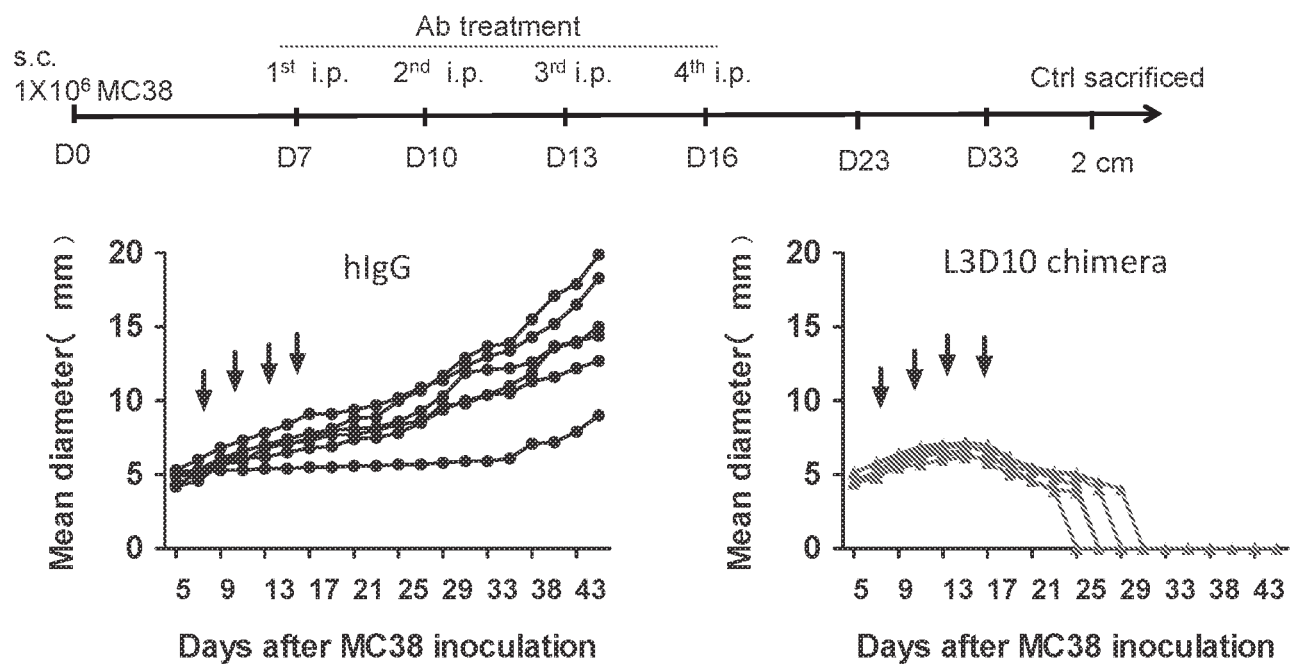


FIG. 12

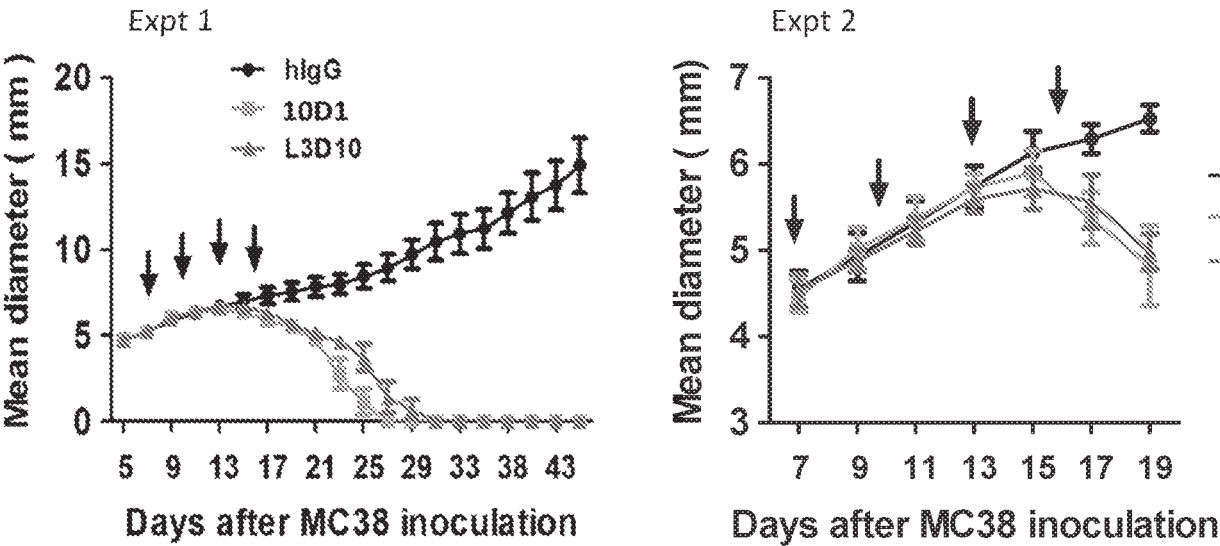


FIG. 13

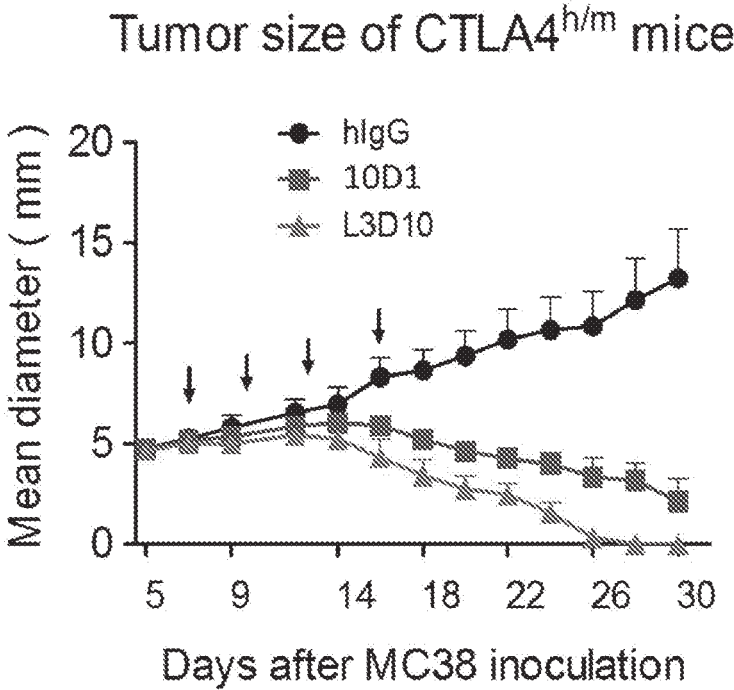


FIG. 14

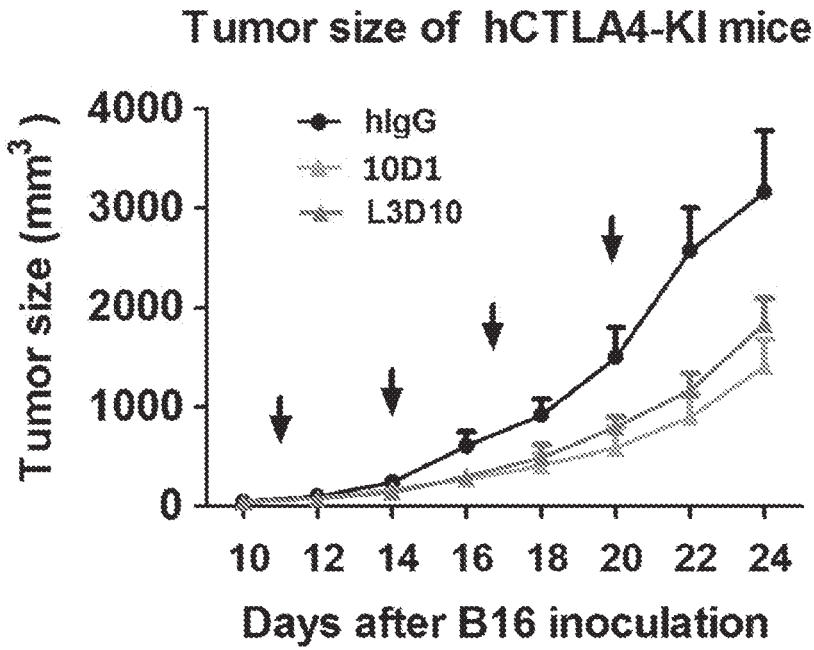


FIG. 15

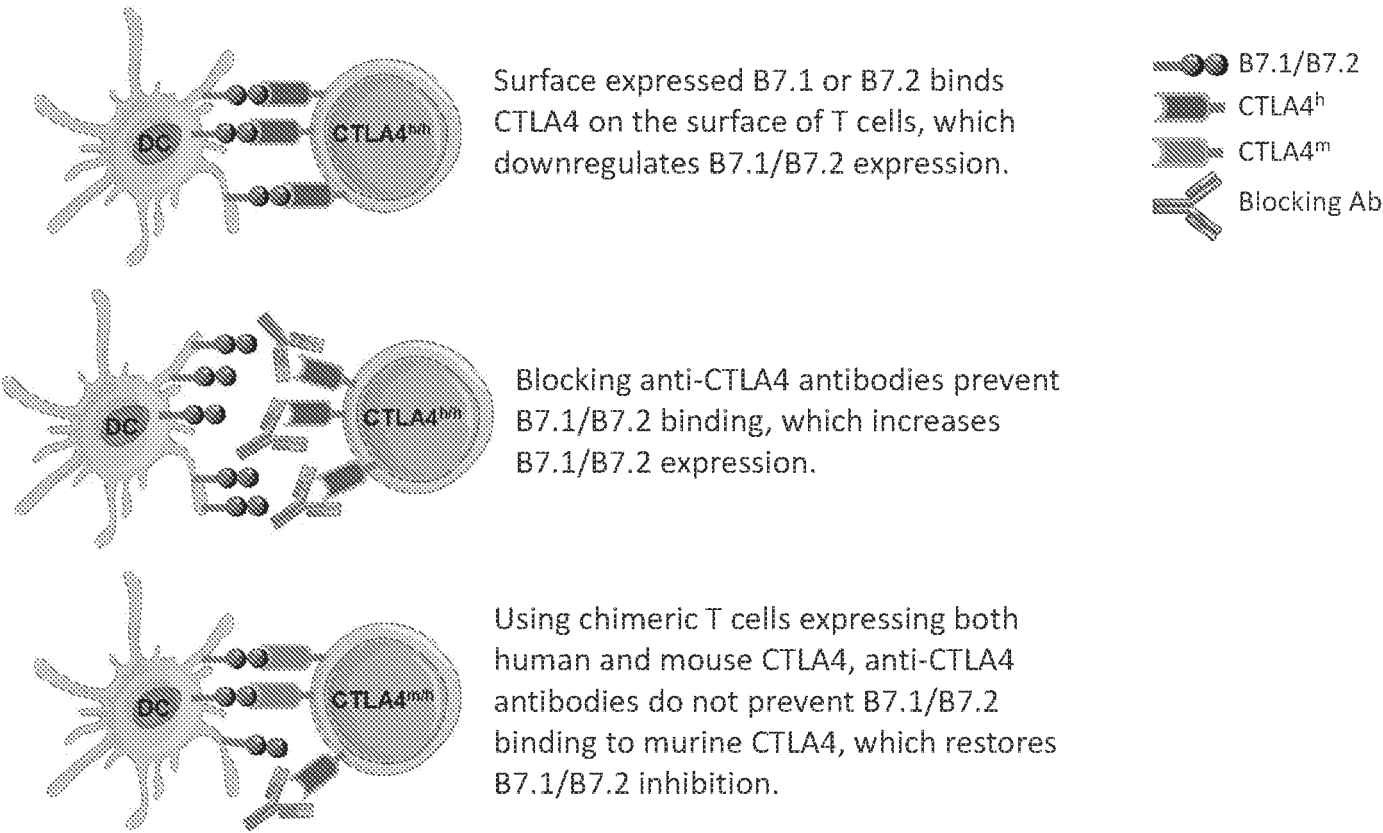
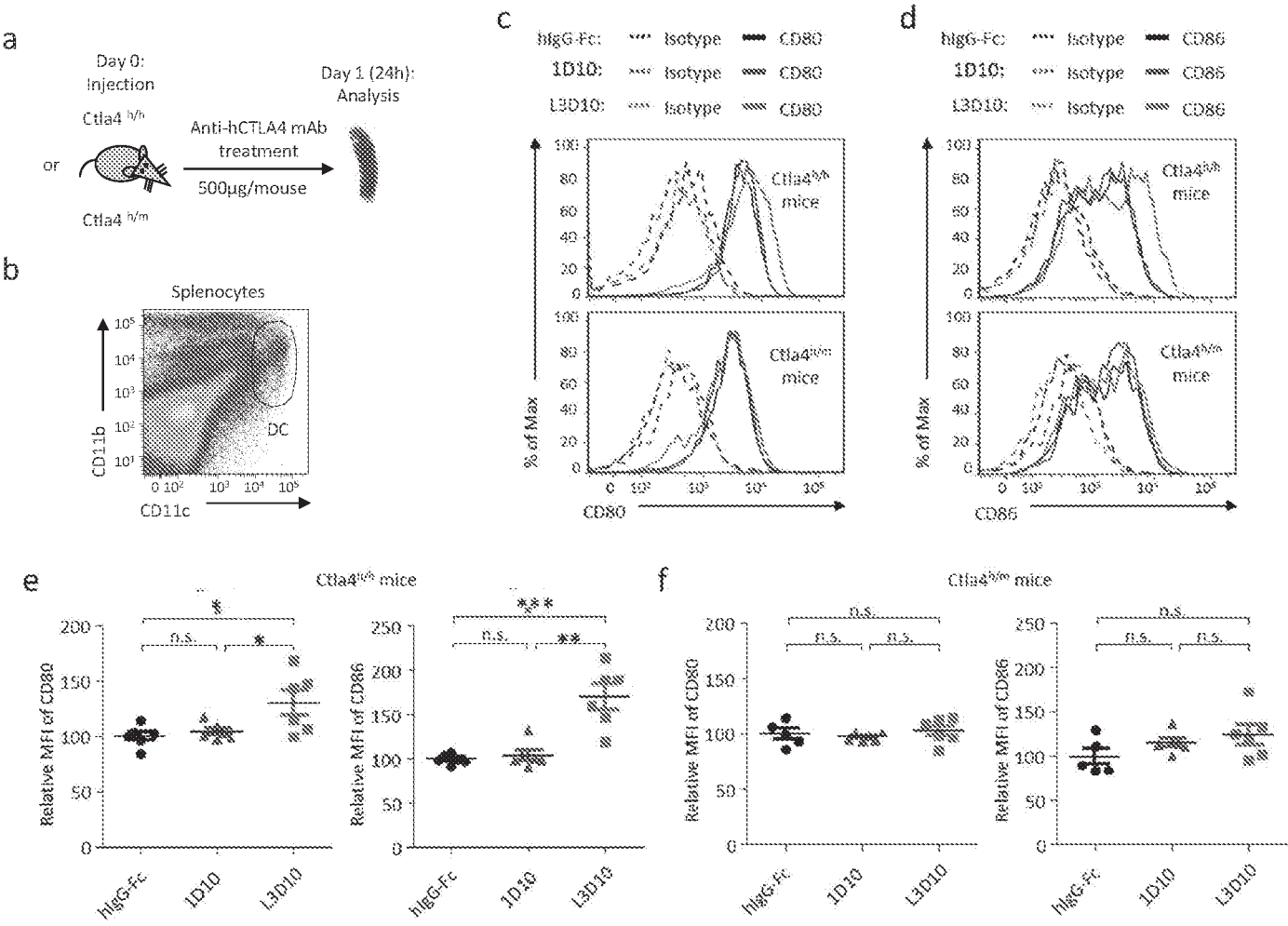


FIG. 16

FIG. 17



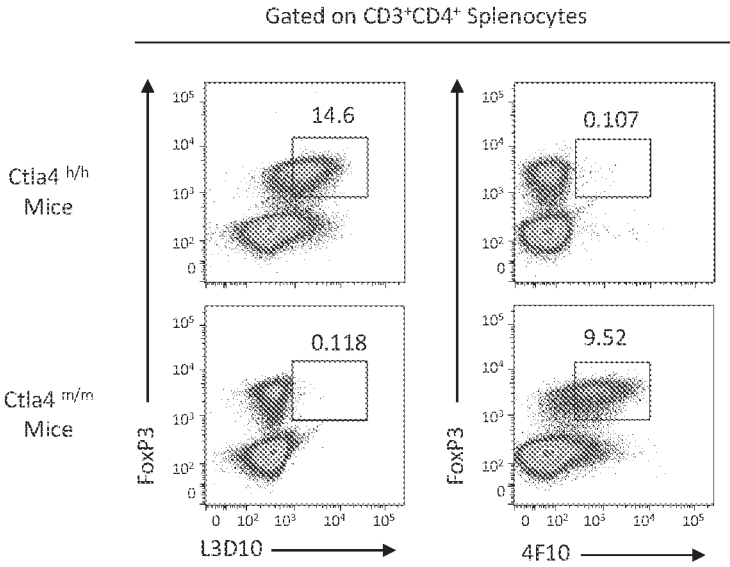


FIG. 18

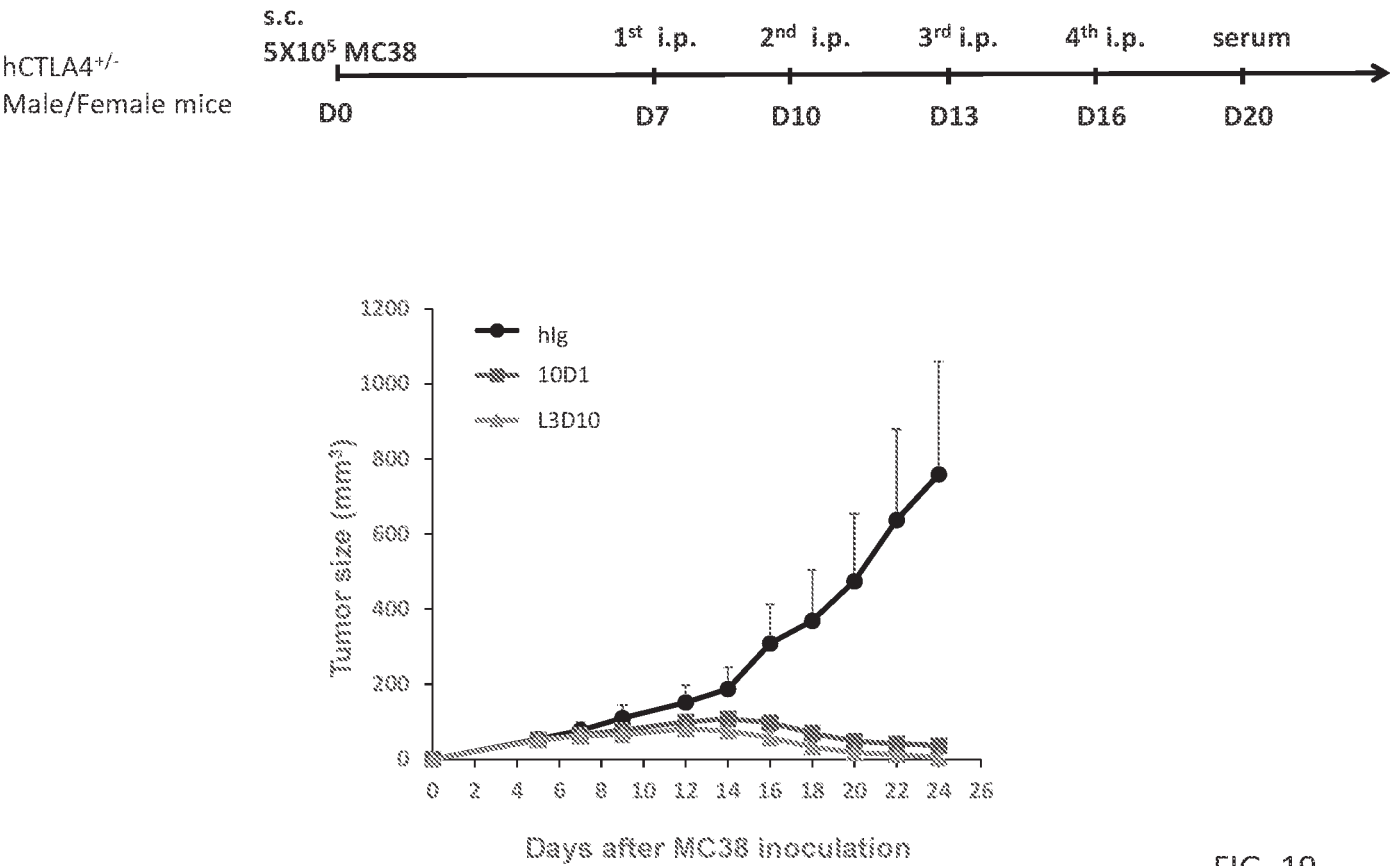


FIG. 19

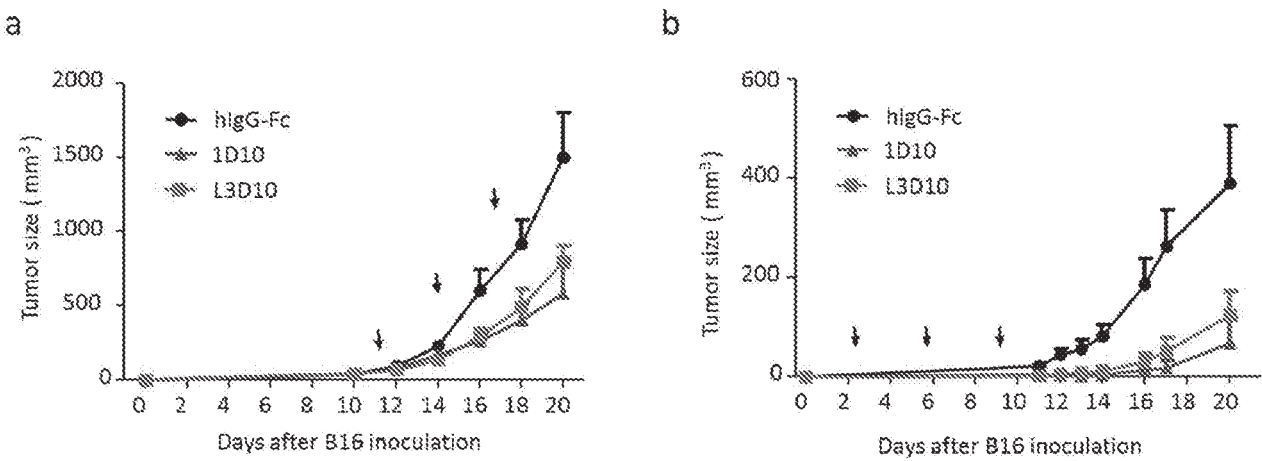


FIG. 20

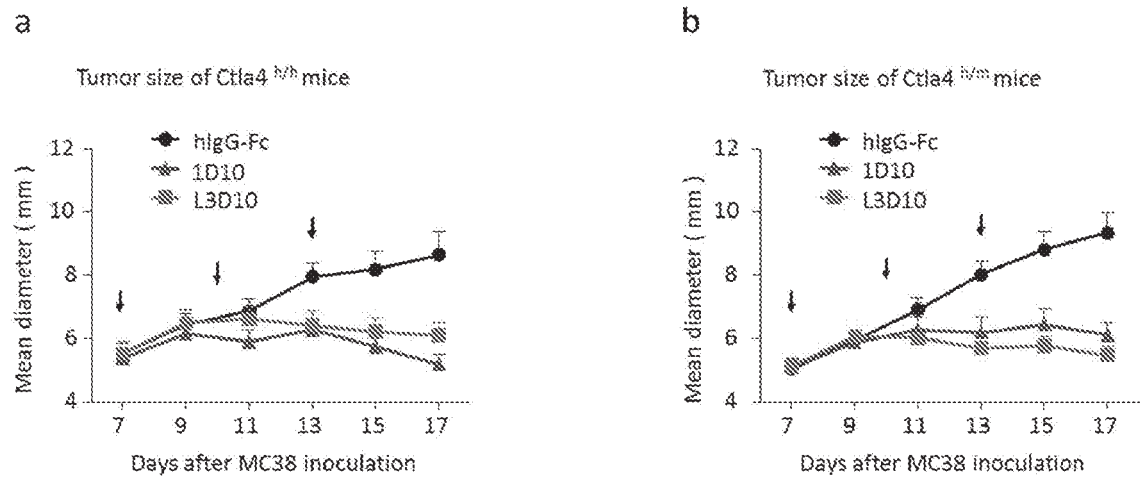


FIG. 21

FIG. 22

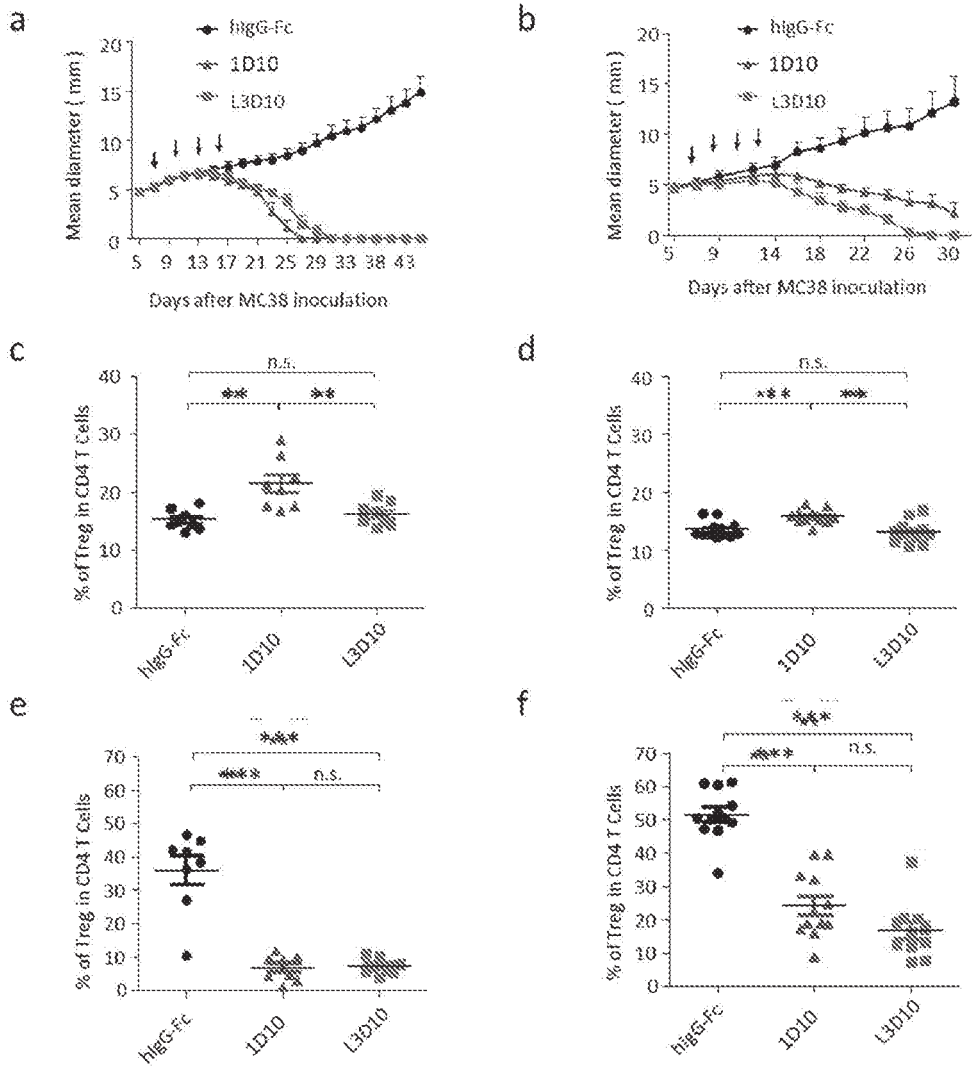
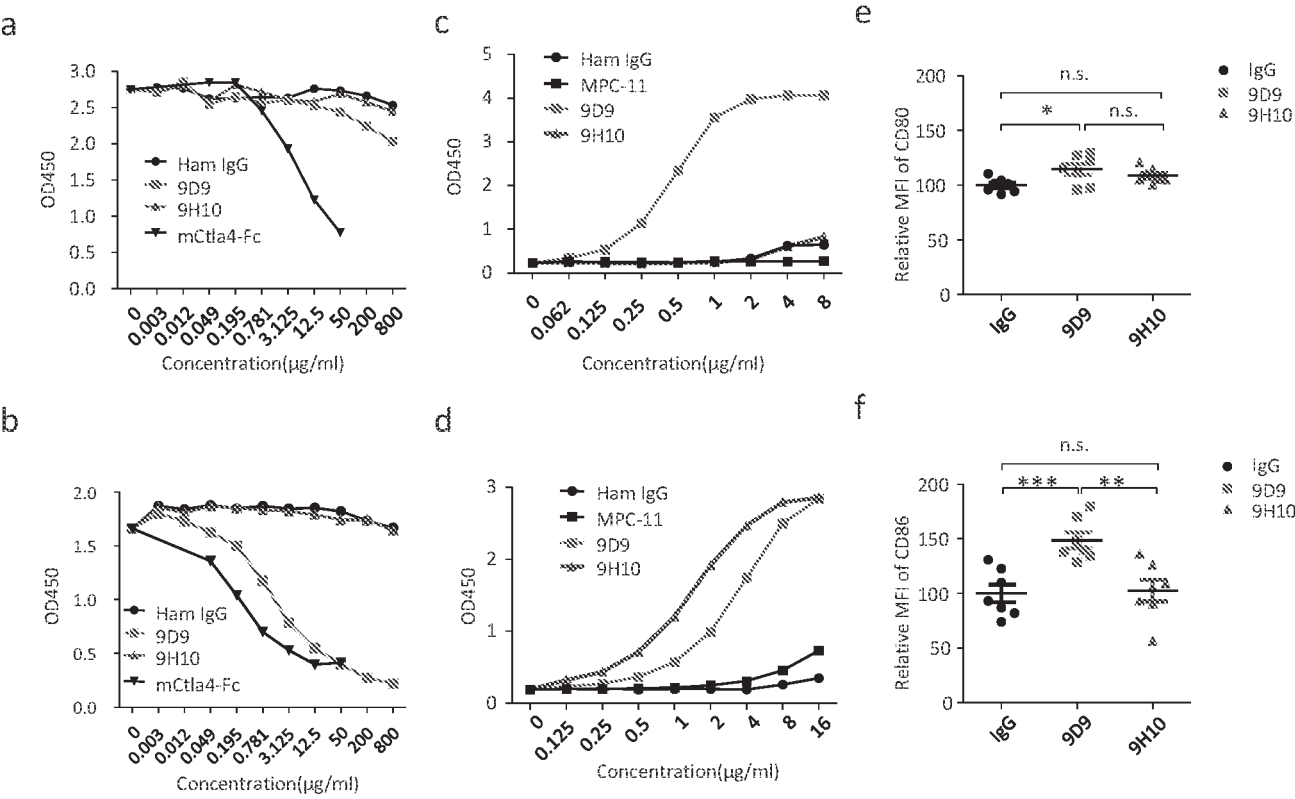


FIG. 23



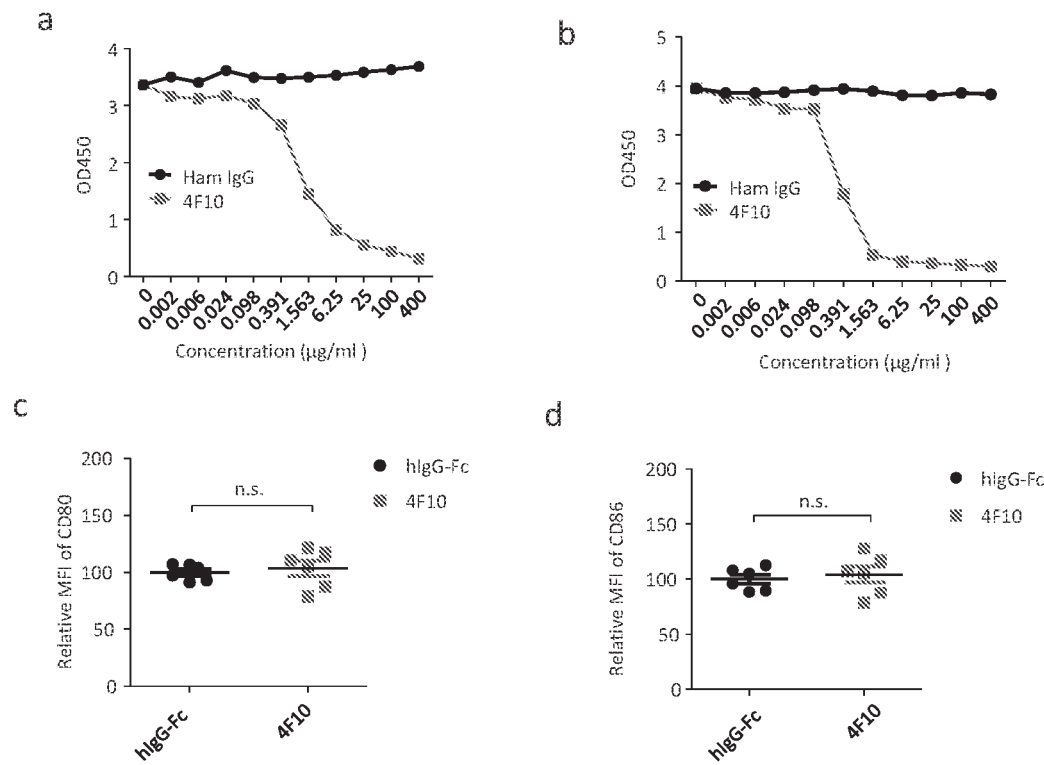


FIG. 24

15 ♀
hCTLA4-KI mice
Day 10

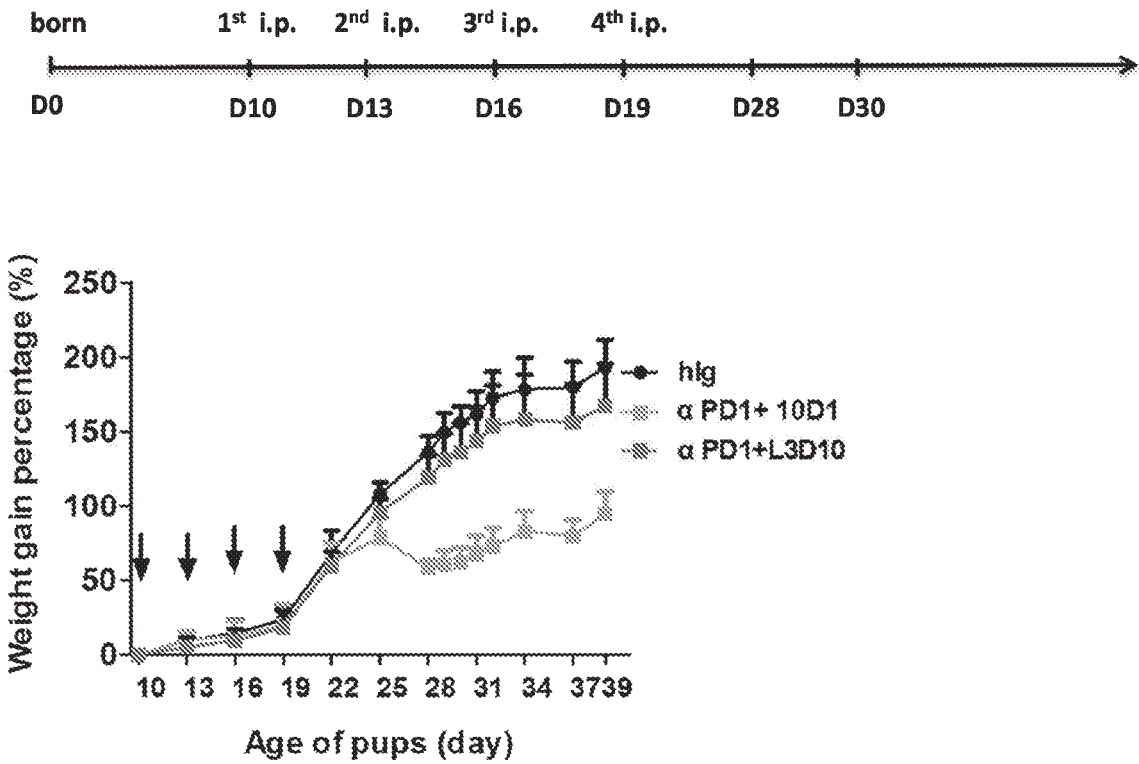


FIG. 25

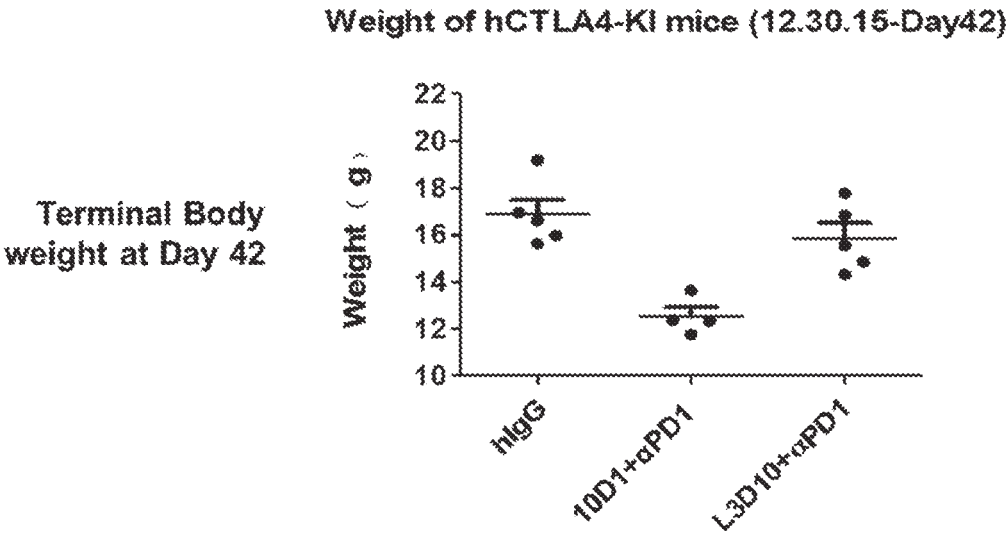
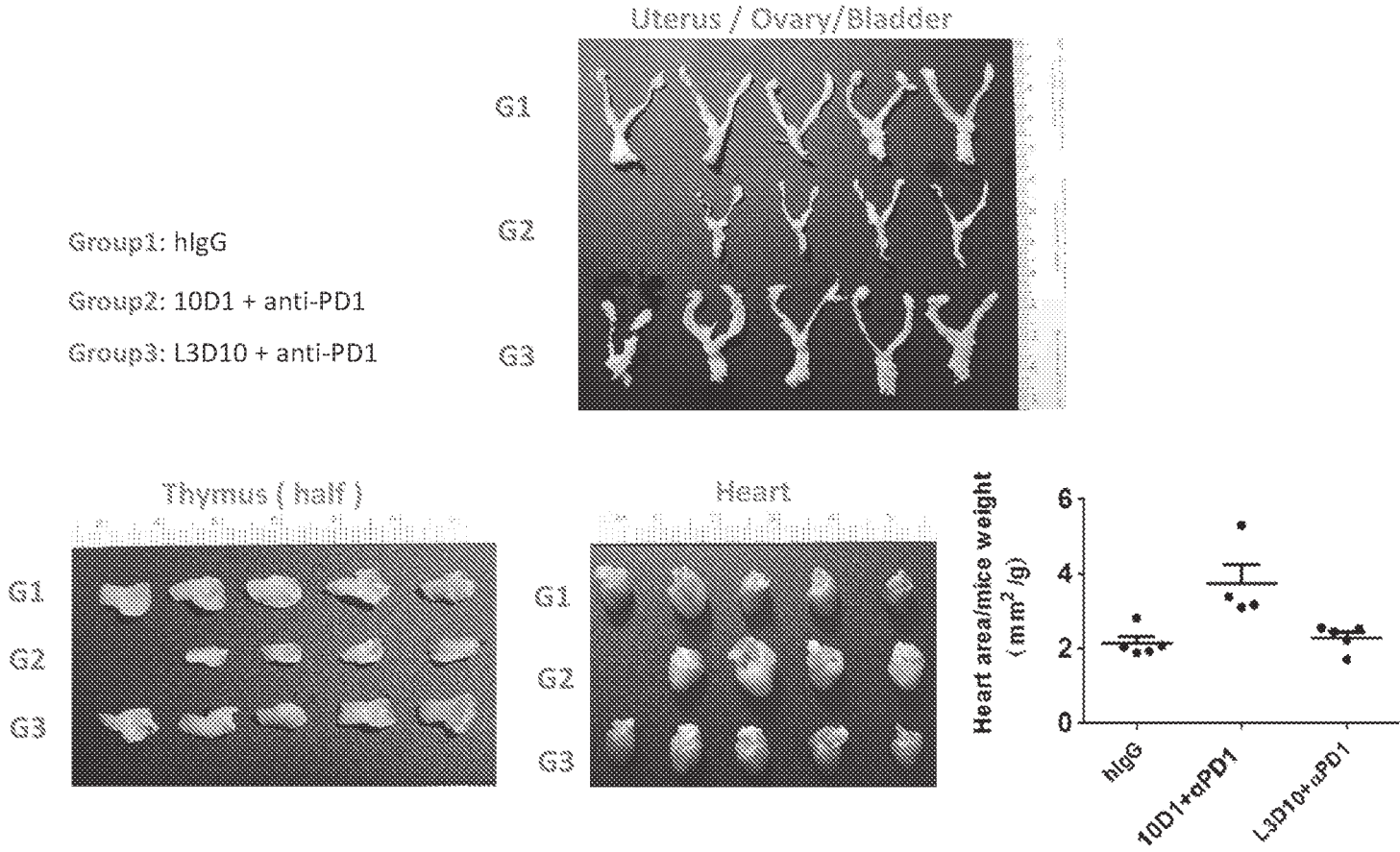


FIG. 26

FIG. 27



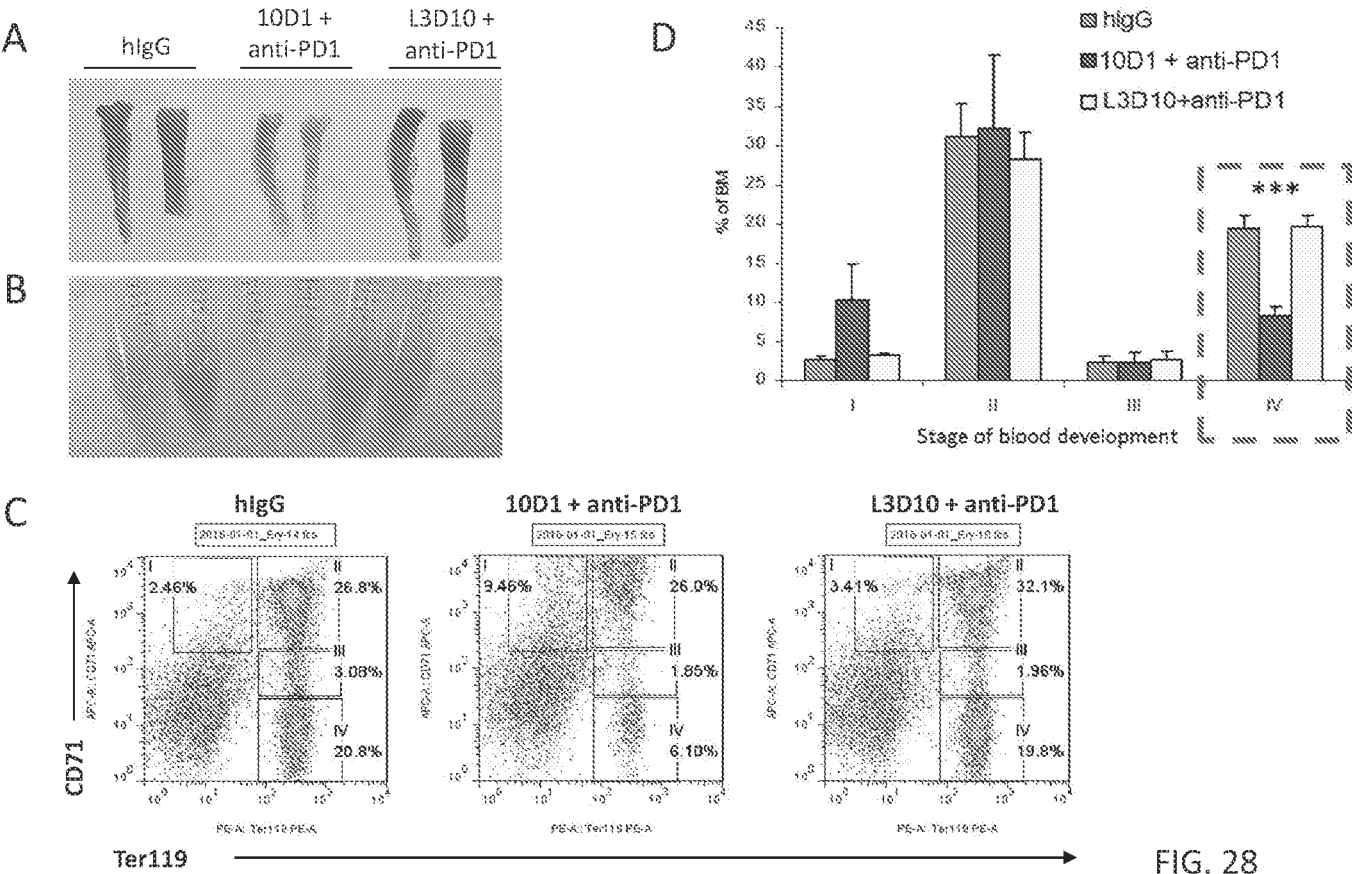


FIG. 28

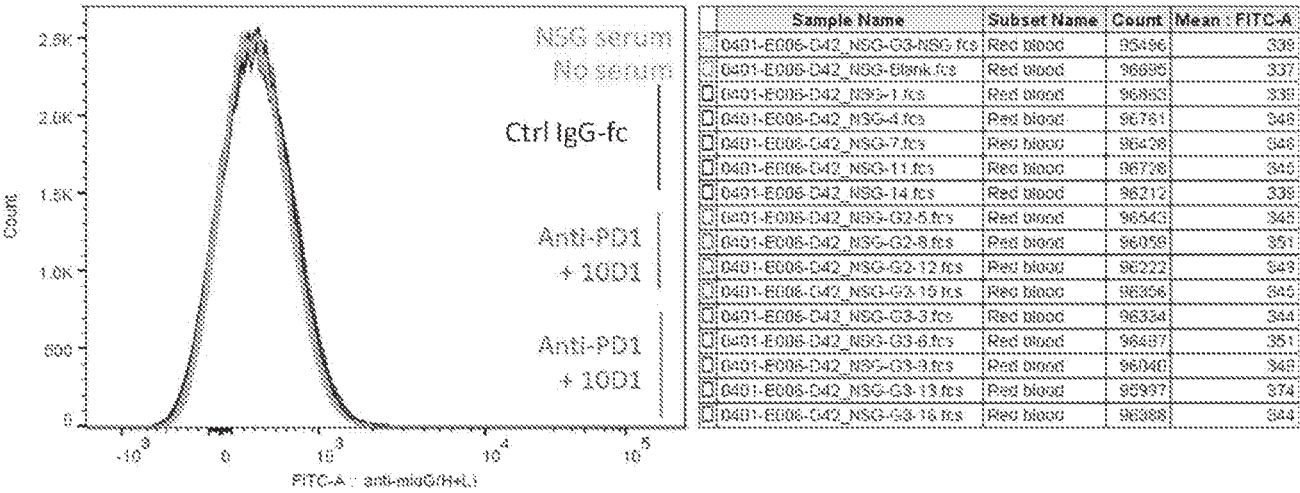


FIG. 29

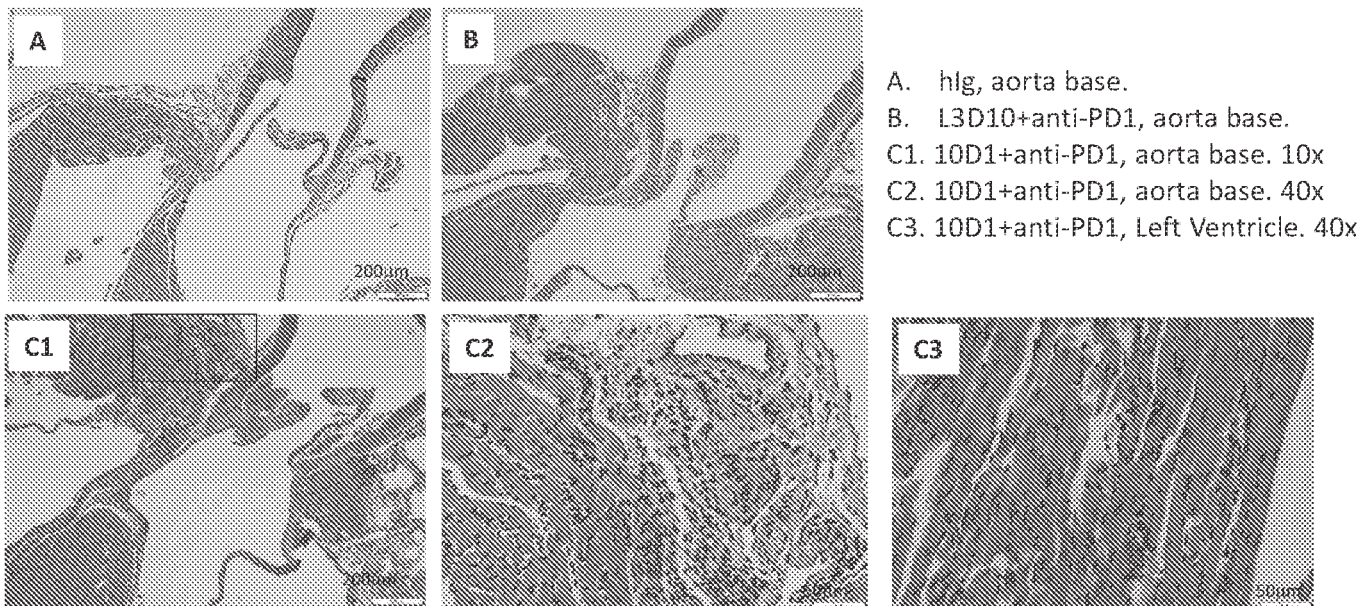


FIG. 30

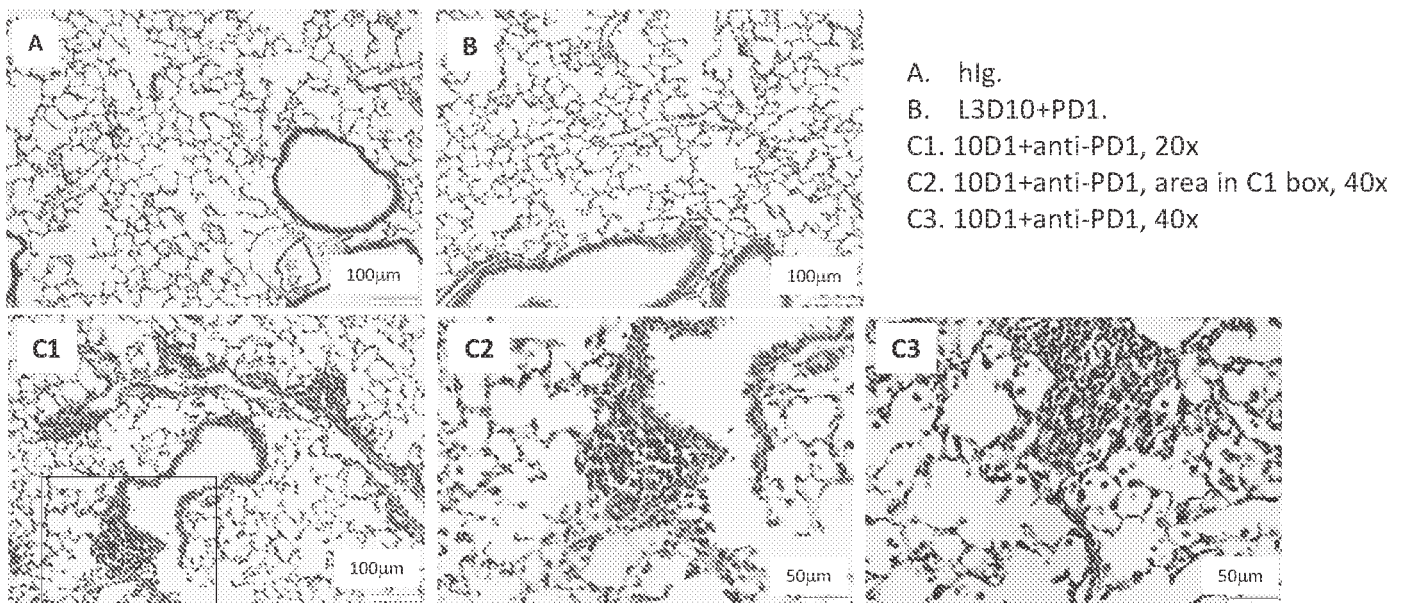


FIG. 31

- A. hlg
- B. L3D10 + anti-PD1
- C. 10D1 + anti-PD1

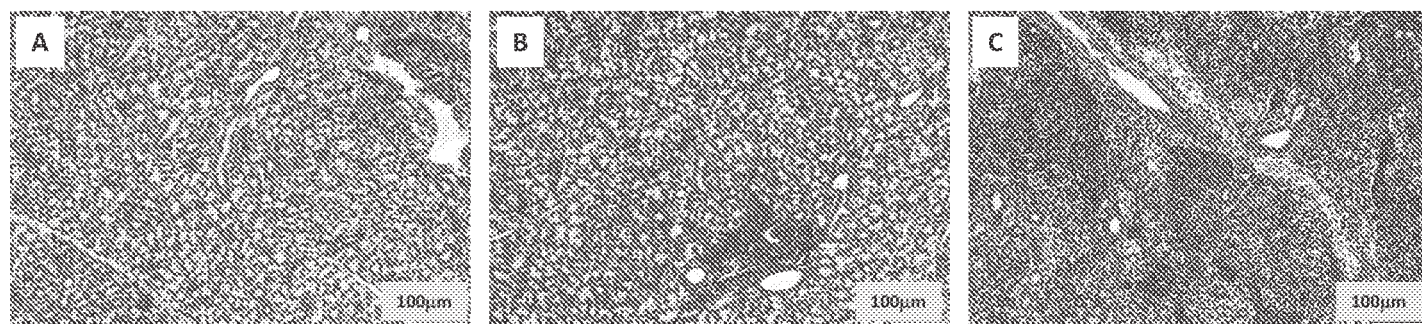


FIG. 32

A-C: Kidney

D-F: Liver

A & D: hlg

B & E: L3D10 + anti-PD1

C & F: 10D1 + anti-PD1

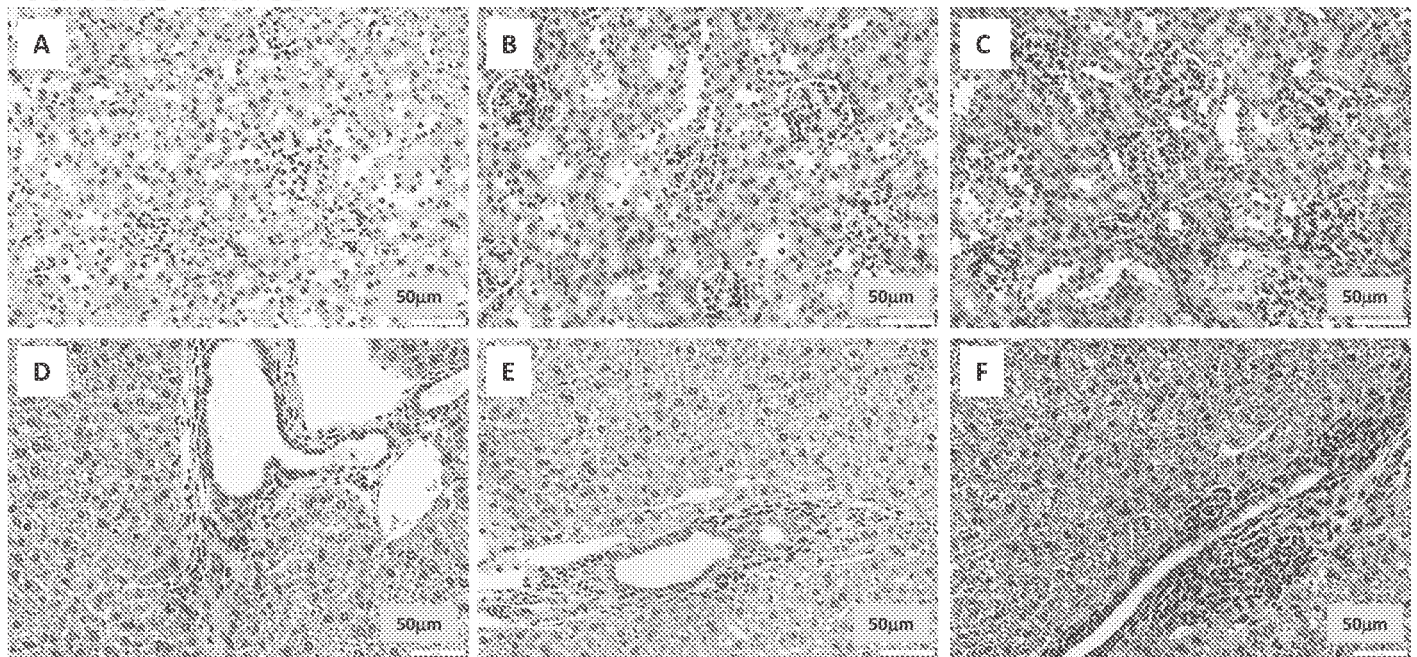


FIG. 33

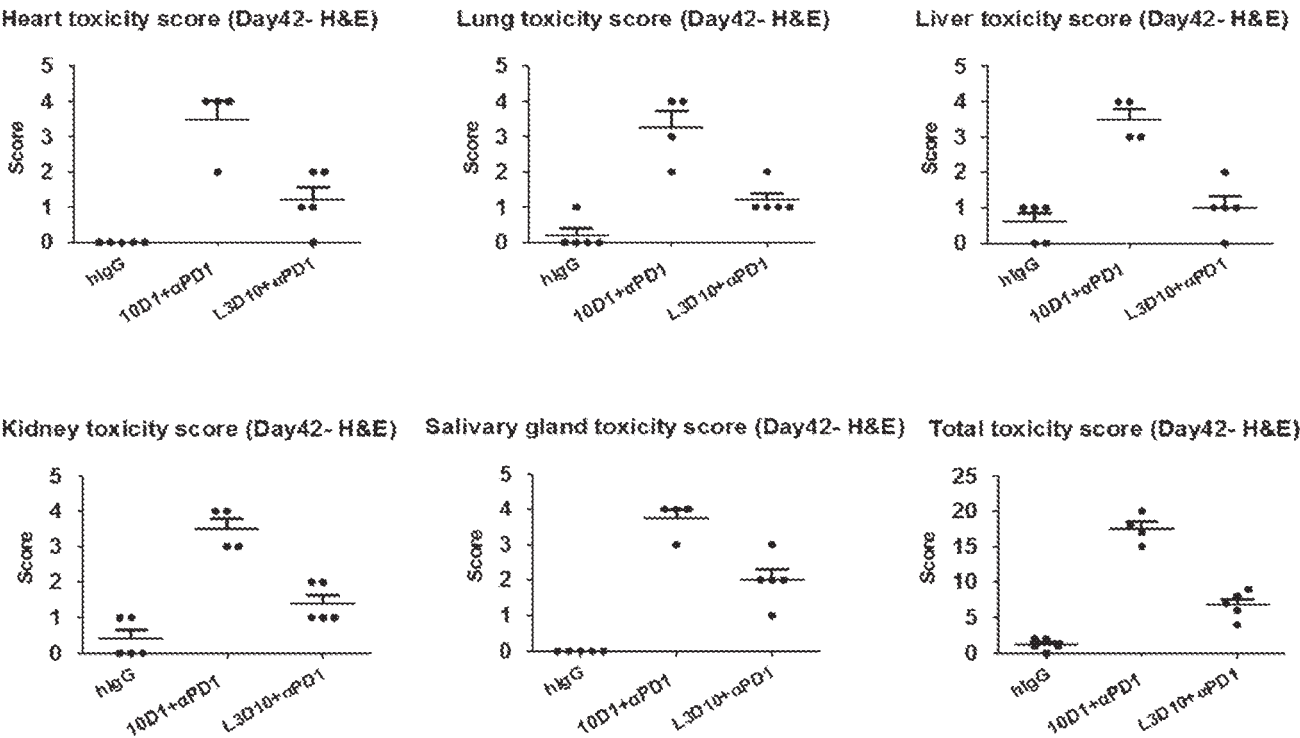


FIG. 34

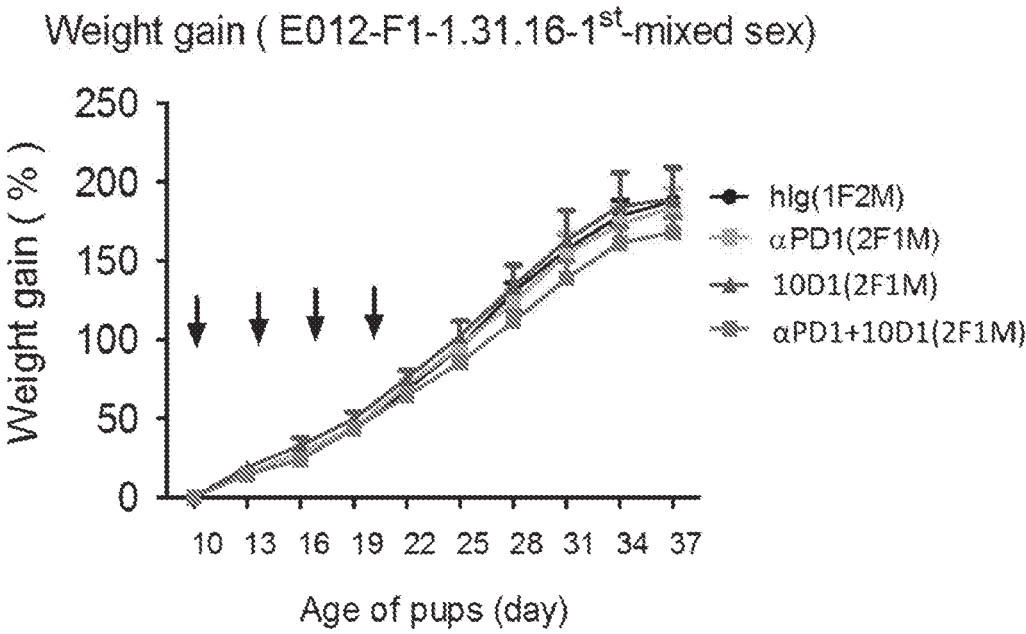


FIG. 35

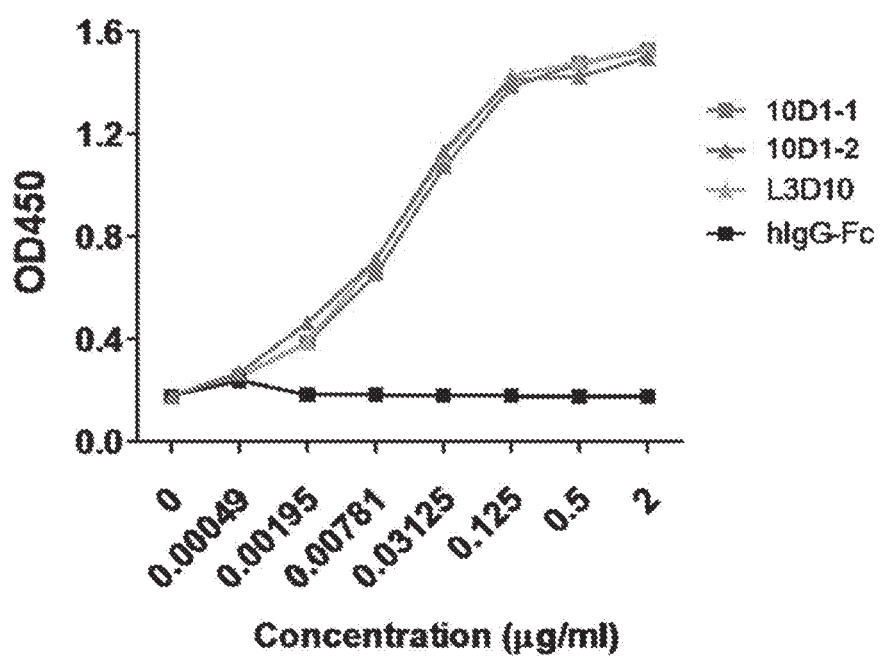


FIG. 36

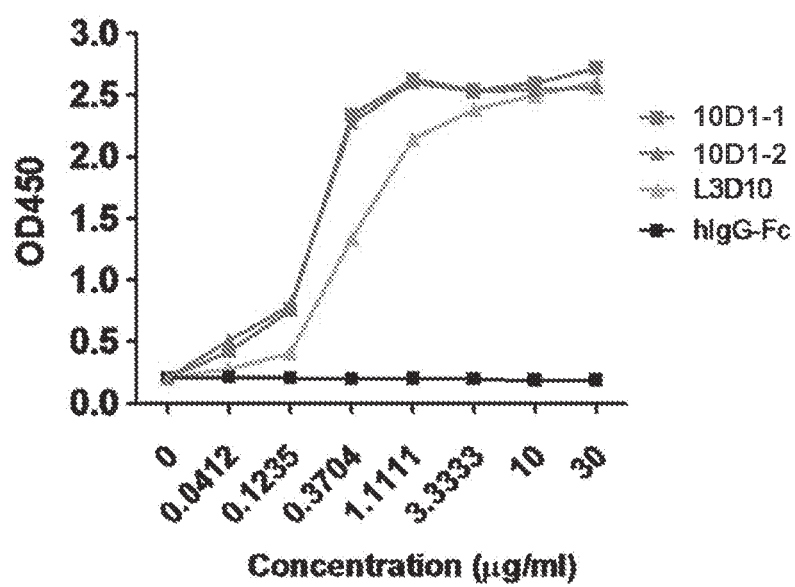


FIG. 37

L3D10 VH amino acid sequence (parental)

QVQLKESGPGLVAPSGSLITCTVSGPRLTFSYGLSWVRQPPGKGLEWLGVTWYDGNTHNPSALXSRLTISKDNSKSOVFLELNSLQDDTATYYCAKTFGHHYGSNFGYYALDHWGQGTSLTVSS

Heavy Chain Framework

QVQLQESGPGLVKPSSETLSLTCTVS WIRQPPGKGLEWIG VTISVDTSKNQFSLKLSSVTAADTAVYYCAR WGQGTSLTVSS

Humanized VH amino acid sequence 1 (HC1)

QVQLQESGPGLVKPSSETLSLTCTVSGPRLTFSYGLSWIRQPPGKGLEWIGYINWYDGNTHNPSALKSRVLTISKDNSKSOVFLELNSLQDDTATYYCAKTFGHHYGSNFGYYALDHWGQGTSLTVSS

Humanized VH amino acid sequence 2 (HC2)

QVQLQESGPGLVKPSSETLSLTCTVSGPRLTFSYGLSWIRQPPGKGLEWIGYINWYDGNTHNPSALKSRVLTISKDNSKSOVFLELNSLQDDTATYYCAKTFGHHYGSNFGYYALDHWGQGTSLTVSS

Humanized VH amino acid sequence 3 (HC3)

QVQLQESGPGLVKPSSETLSLTCTVSGPRLTFSYGLSWIRQPPGKGLEWIGYINWYDGNTHNPSALKSRVLTISVDTSKNQFSLKLSSVTAADTAVYYCAKTFGHHYGSNFGYYALDHWGQGTSLTVSS

L3D10 VL amino acid sequence (parental)

DIQMTQSPASLSVSGDETVTITCRASENIYGNLAWYQQKQKSPQLLVYANNLADGVPSRFGSGSGTDFTLTISSLQPEDFATYYCQHLWGTFPYTFGGGTKLEIK

Light Chain Framework

DIQMTQSPSSLSASVGDRTITC WYQQKPGKAPKLLIY GVPSRFGSGSGTDFTLTISSLQPEDFATYYC FGQGTKLEIK

Humanized VL amino acid sequence 1 (LC1)

DIQMTQSPSSLSASVGDRTITCRASENIYGNLAWYQQKPGKAPKLLIYAASTNQSGVPSRFGSGSGTDFTLTISSLQPEDFATYYCQHLWGTFPYTFGGGTKLEIK

Humanized VL amino acid sequence 2 (LC2)

DIQMTQSPSSLSASVGDRTITCRASENIYGNLAWYQQKPGKAPKLLIYAASTNQSGVPSRFGSGSGTDFTLTISSLQPEDFATYYCQHLWGTFPYTFGGGTKLEIK

Humanized VL amino acid sequence 3 (LC3)

DIQMTQSPSSLSASVGDRTITCRASENIYGNLAWYQQKPGKAPKLLIYAASTNQSGVPSRFGSGSGTDFTLTISSLQPEDFATYYCQHLWGTFPYTFGGGTKLEIK

FIG. 38

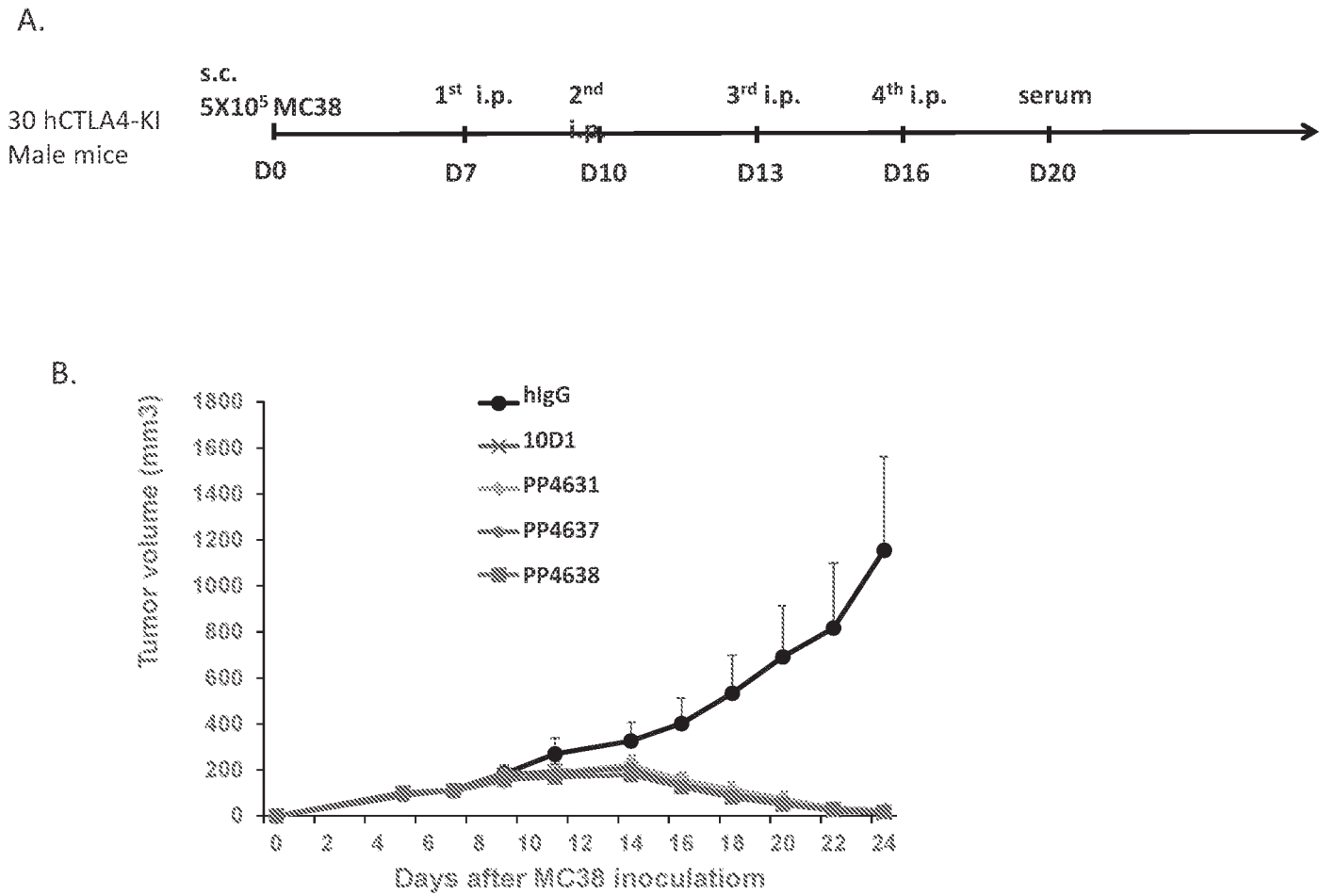


FIG. 39

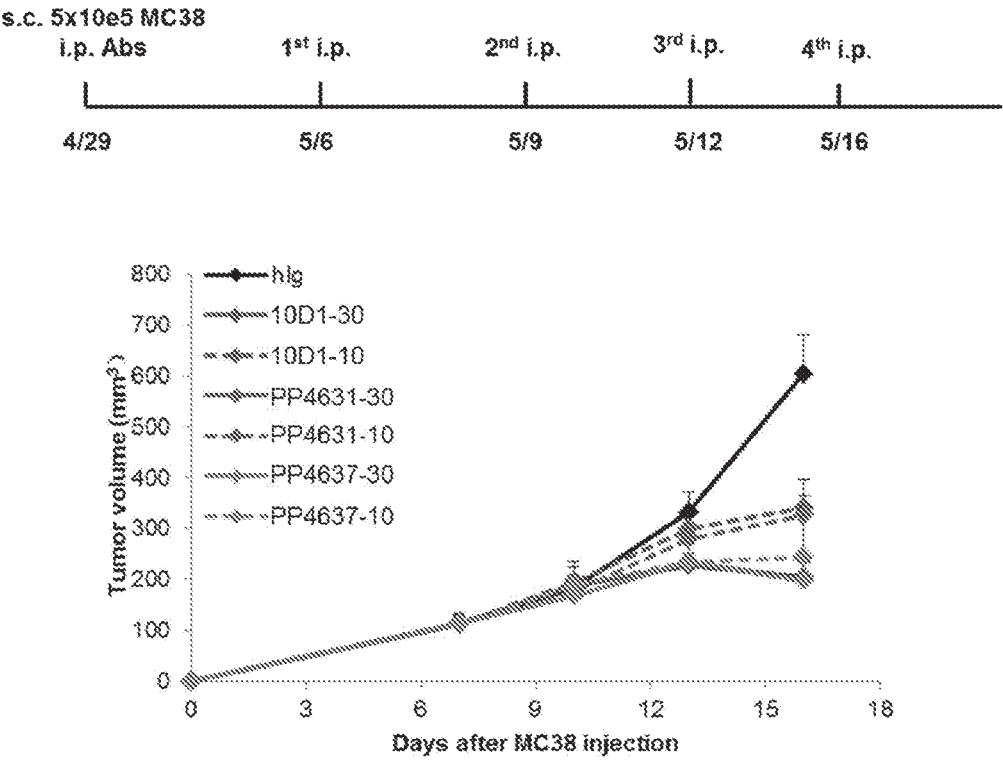


FIG. 40

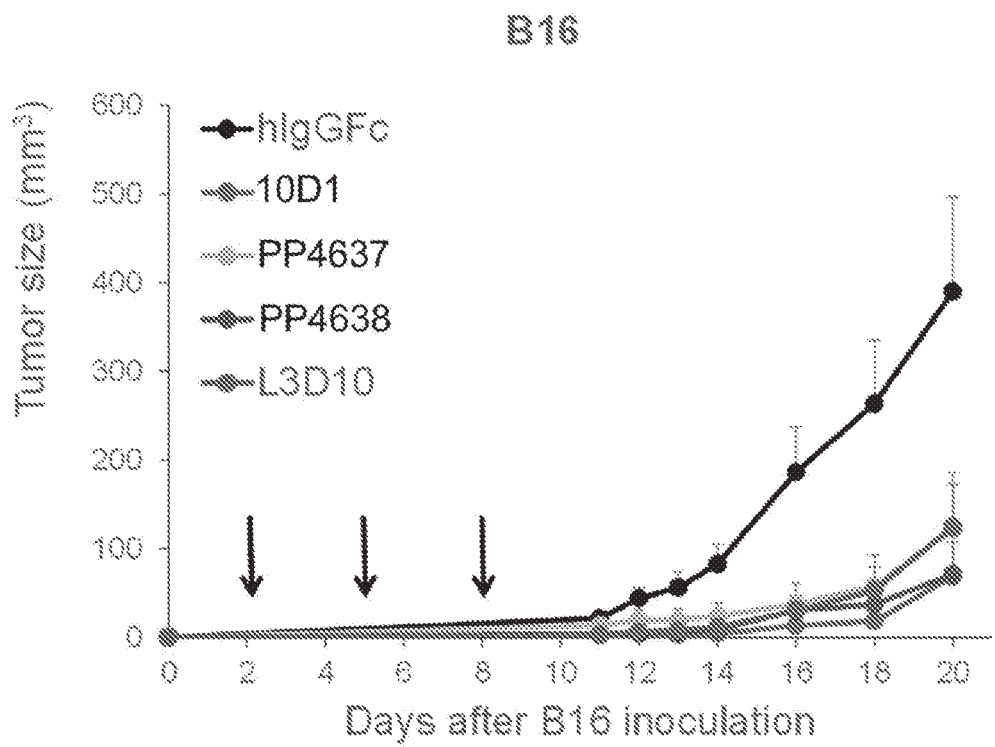


FIG. 41

hlg VS α PD1+L3D10	P value = 0.16
hlg VS α PD1+hlq	P value = 0.0384*
hlg VS α PD1+10D1	P value = $<2e-16^{***}$
hlg VS α PD1+PP4631	P value = 0.16
hlg VS α PD1+PP4637	P value = 0.00207**
α PD1+L3D10 VS α PD1+hlq	P value = 0.00654**
α PD1+L3D10 VS α PD1+10D1	P value = $<2e-16^{***}$
α PD1+L3D10 VS α PD1+PP4631	P value = 0.492
α PD1+L3D10 VS α PD1+PP4637	P value = 0.000124***
α PD1+hlq VS α PD1+10D1	P value = $<2e-16^{***}$
α PD1+hlq VS α PD1+PP4631	P value = 0.0579
α PD1+hlq VS α PD1+PP4637	P value = 0.409
α PD1+10D1 VS α PD1+PP4631	P value = $<2e-16^{***}$
α PD1+10D1 VS α PD1+PP4637	P value = $<2e-16^{***}$
α PD1+PP4631 VS α PD1+PP4637	P value = 0.000446***

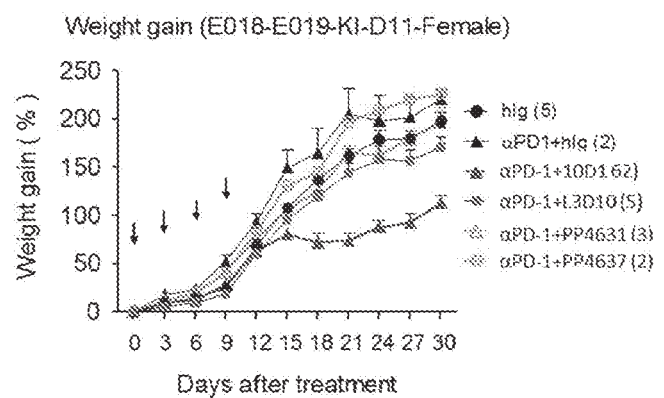


FIG. 42

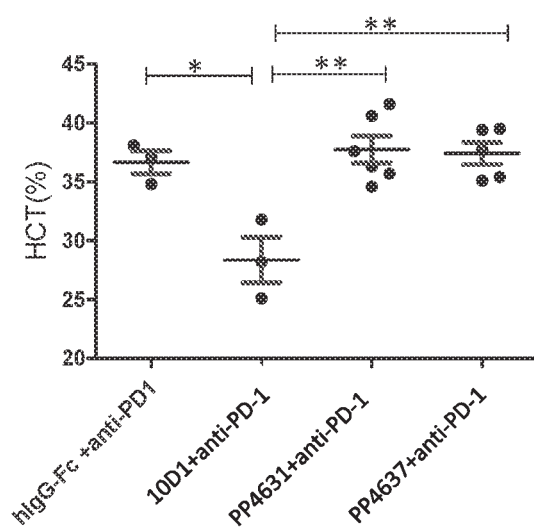


FIG. 43

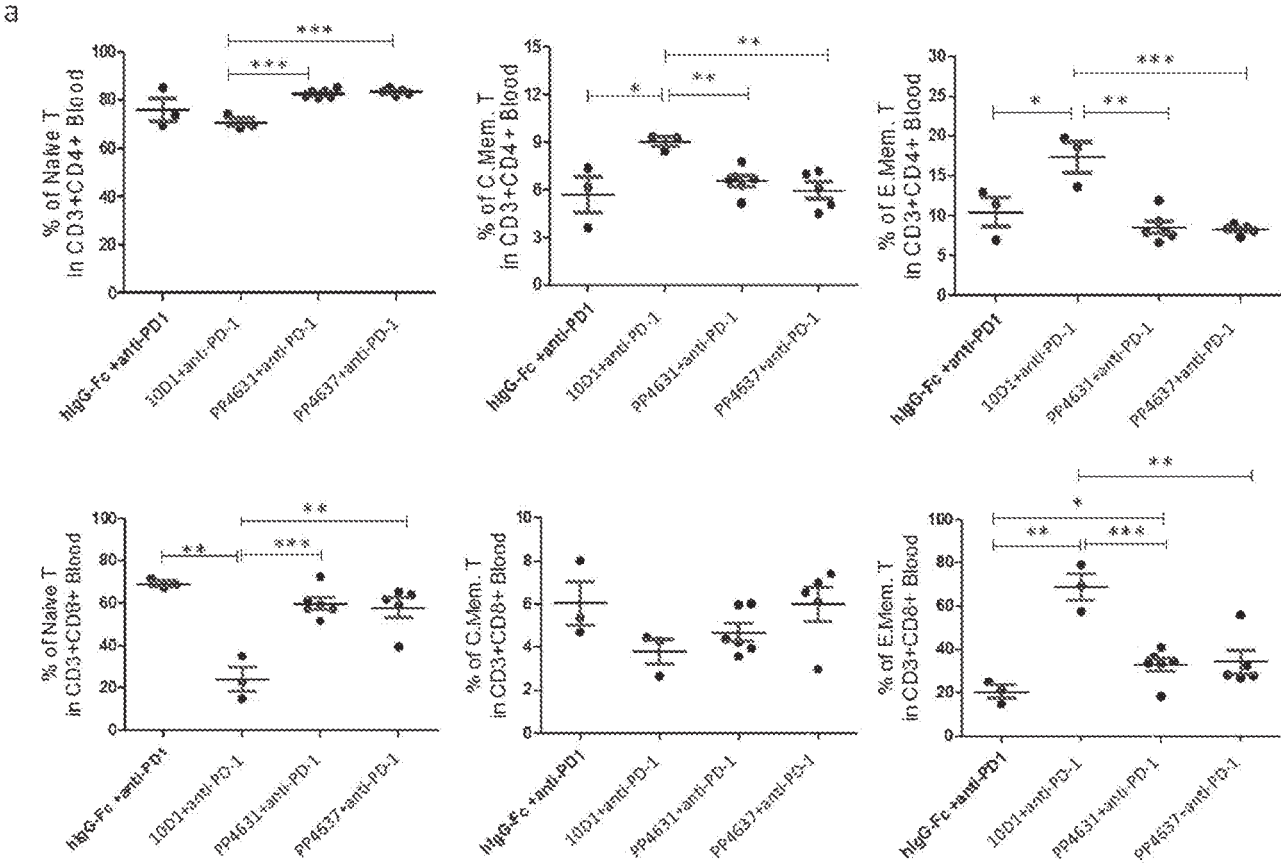


FIG. 44A

b

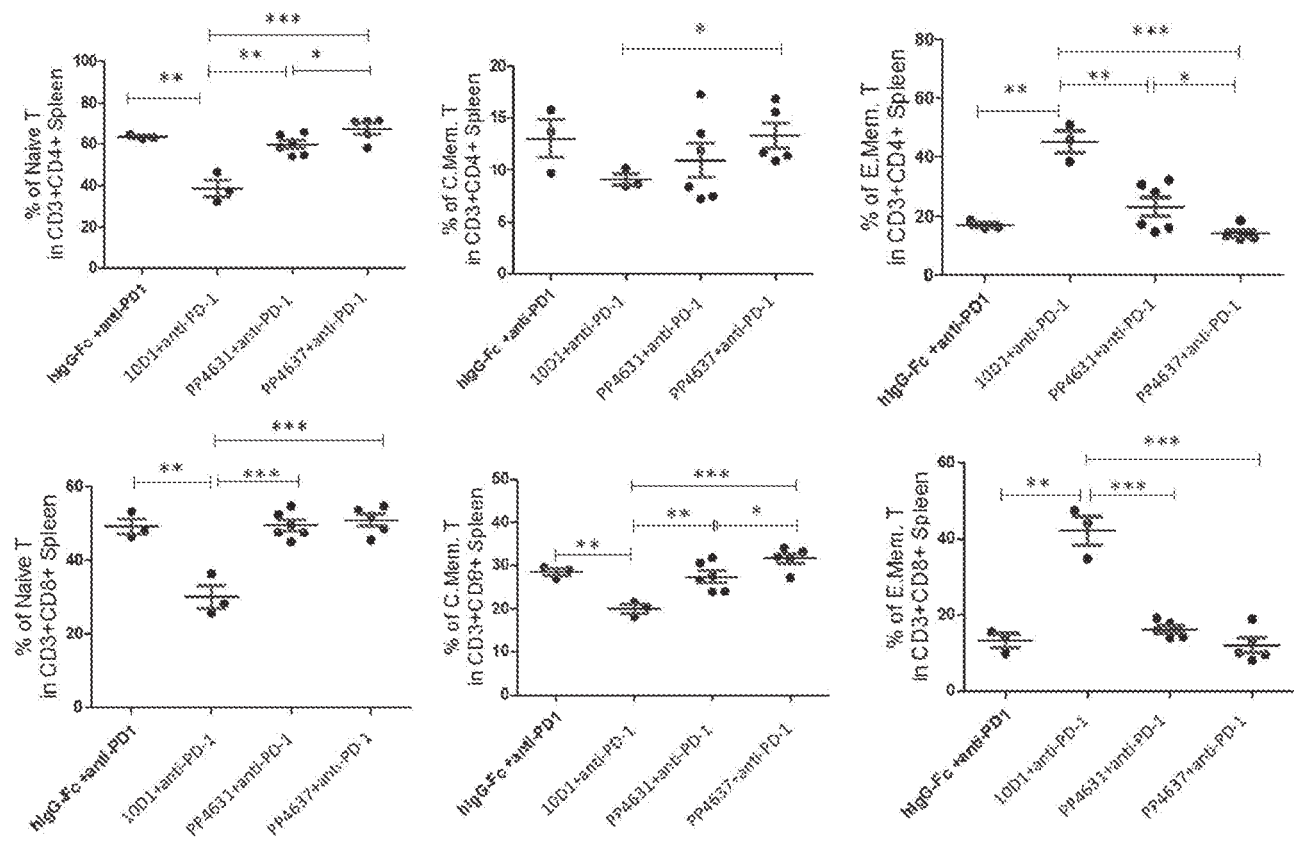


FIG. 44B

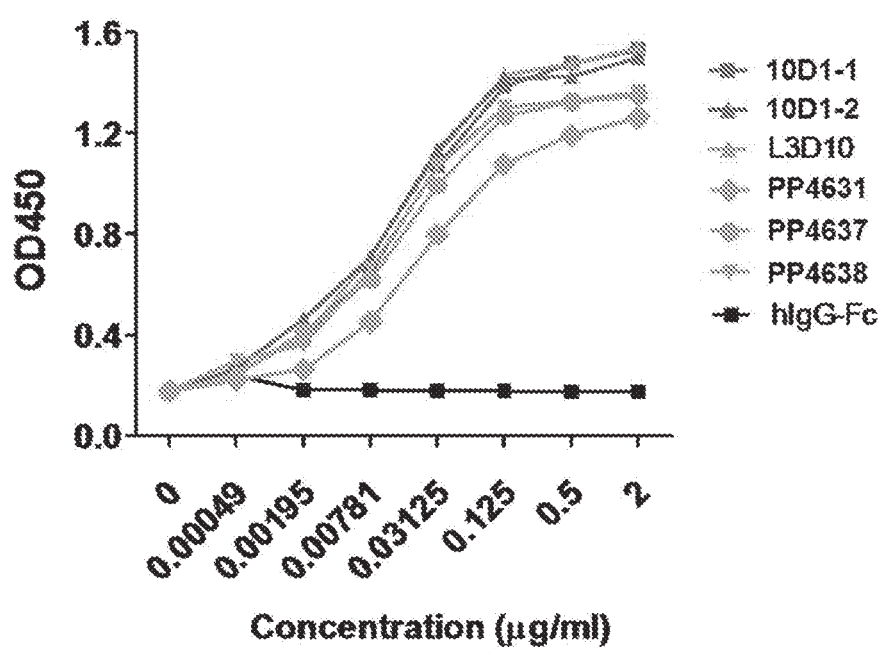


FIG. 45

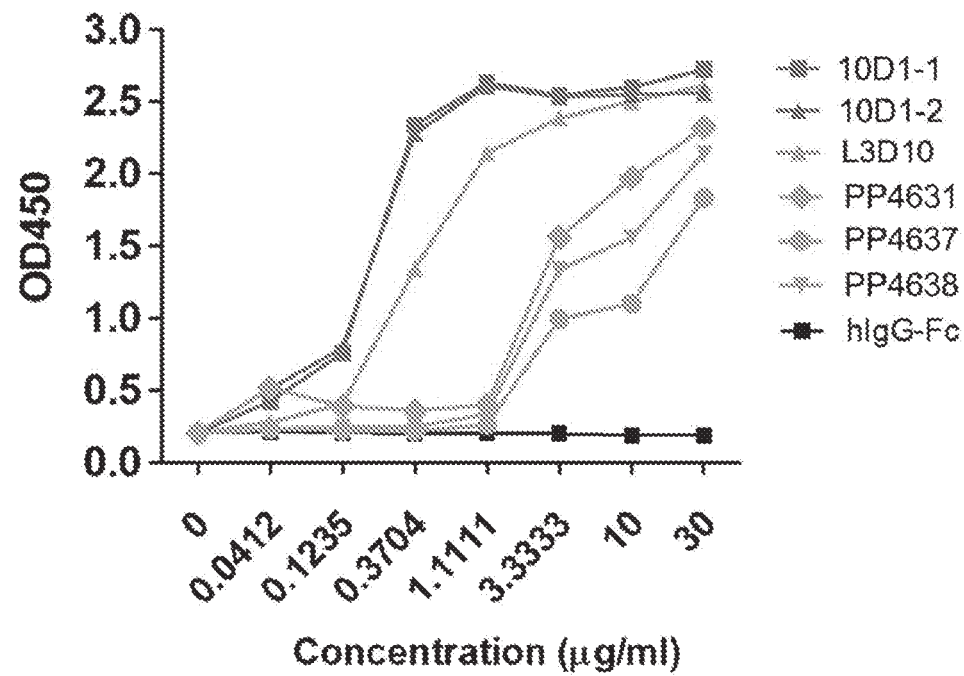


FIG. 46

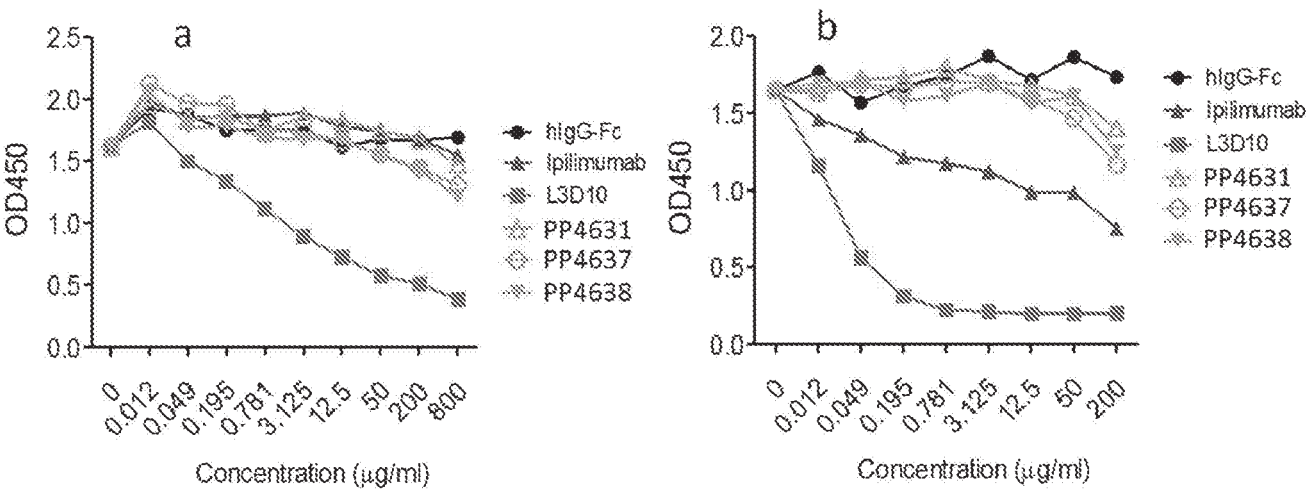


FIG. 47

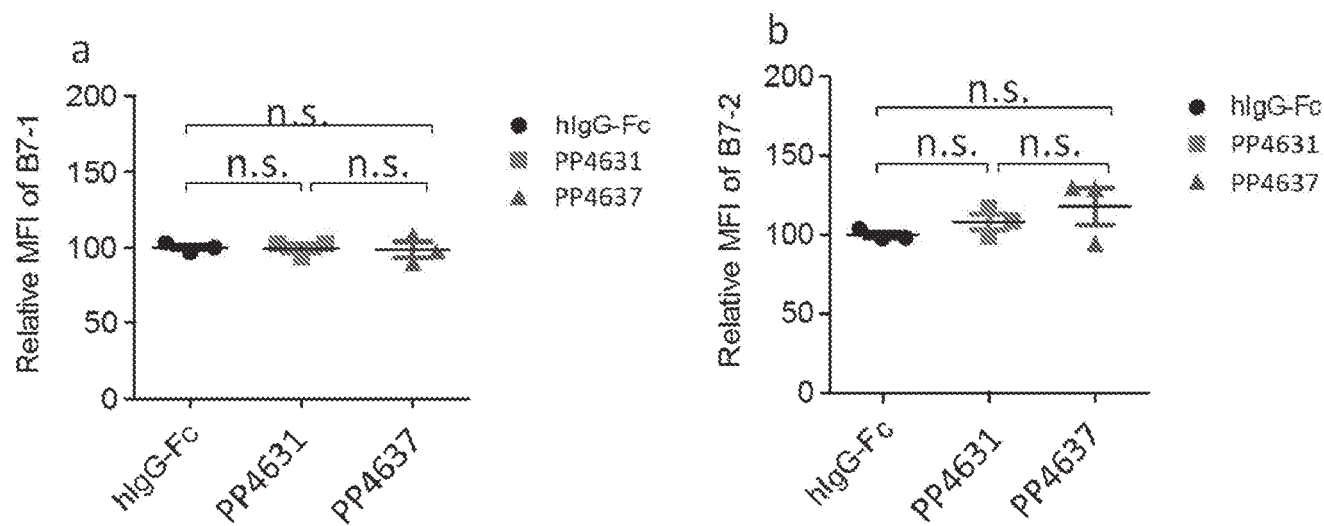


FIG. 48

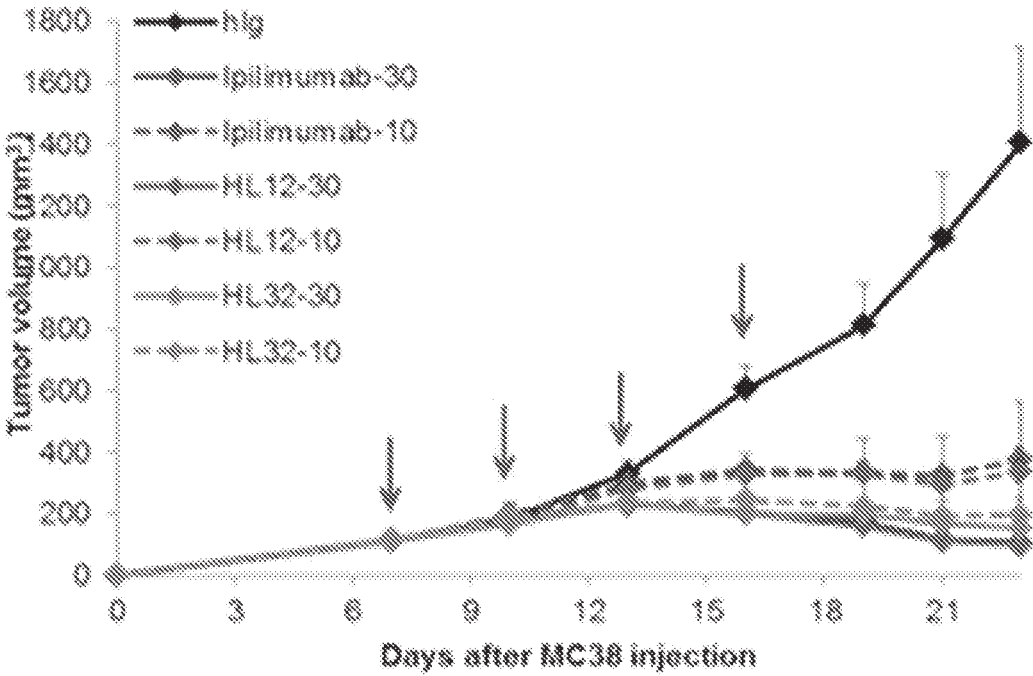


FIG. 49

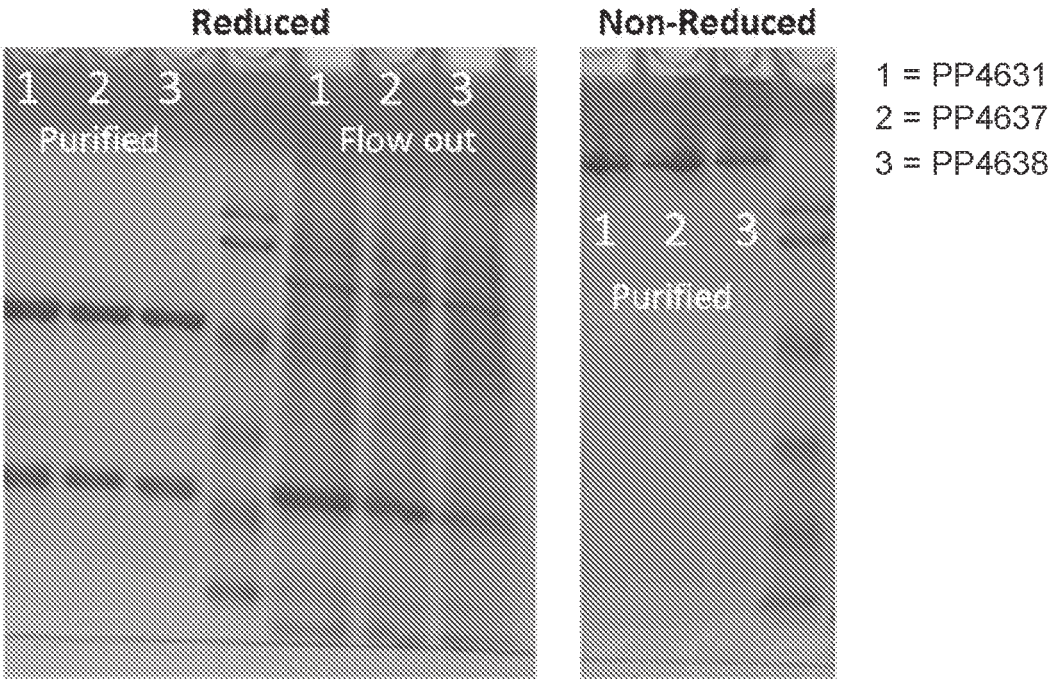
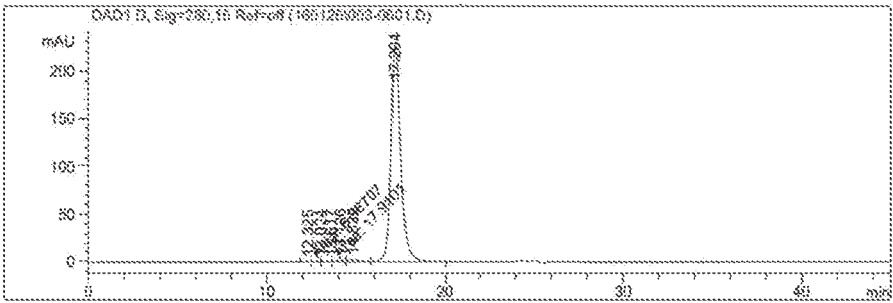


FIG. 50

PP4631



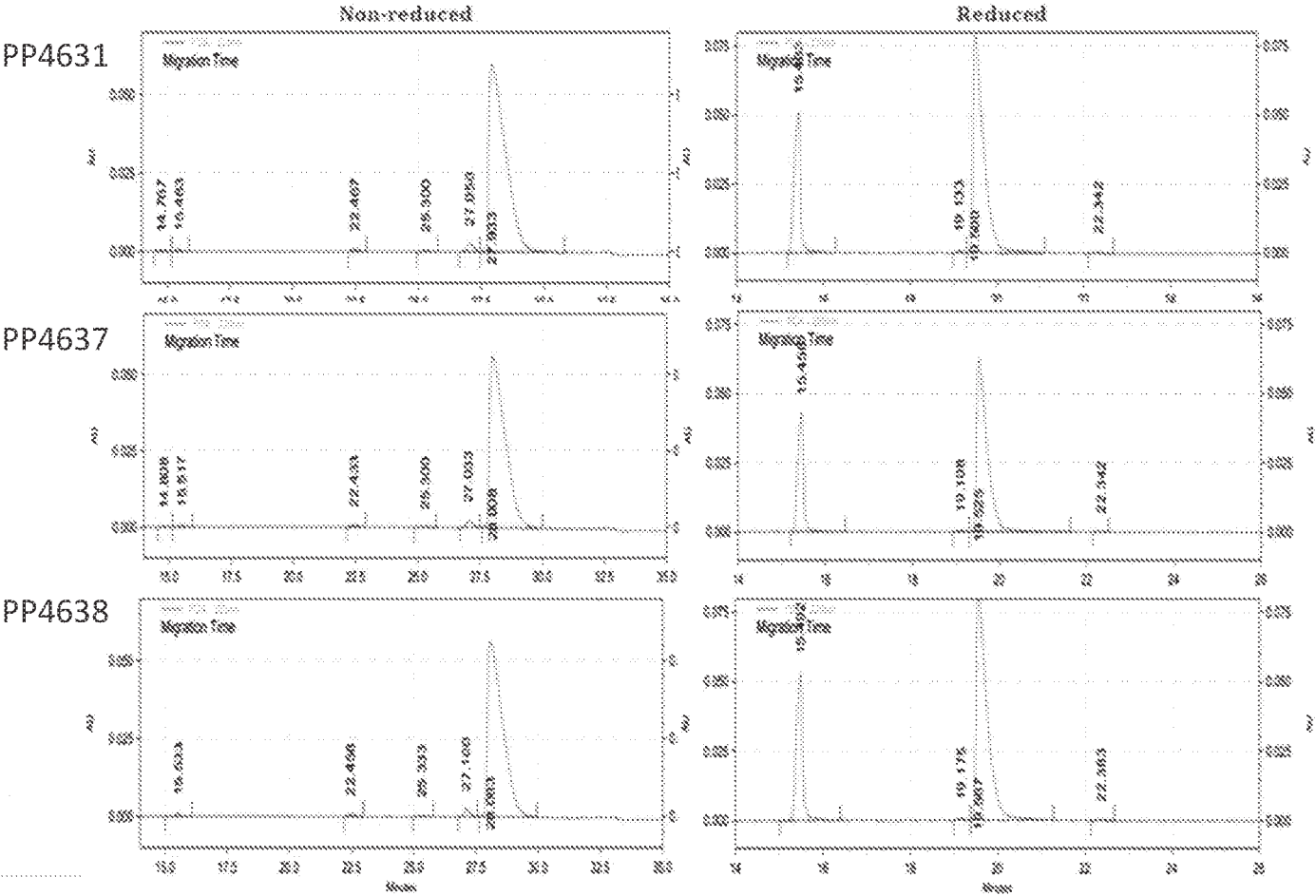


FIG. 52

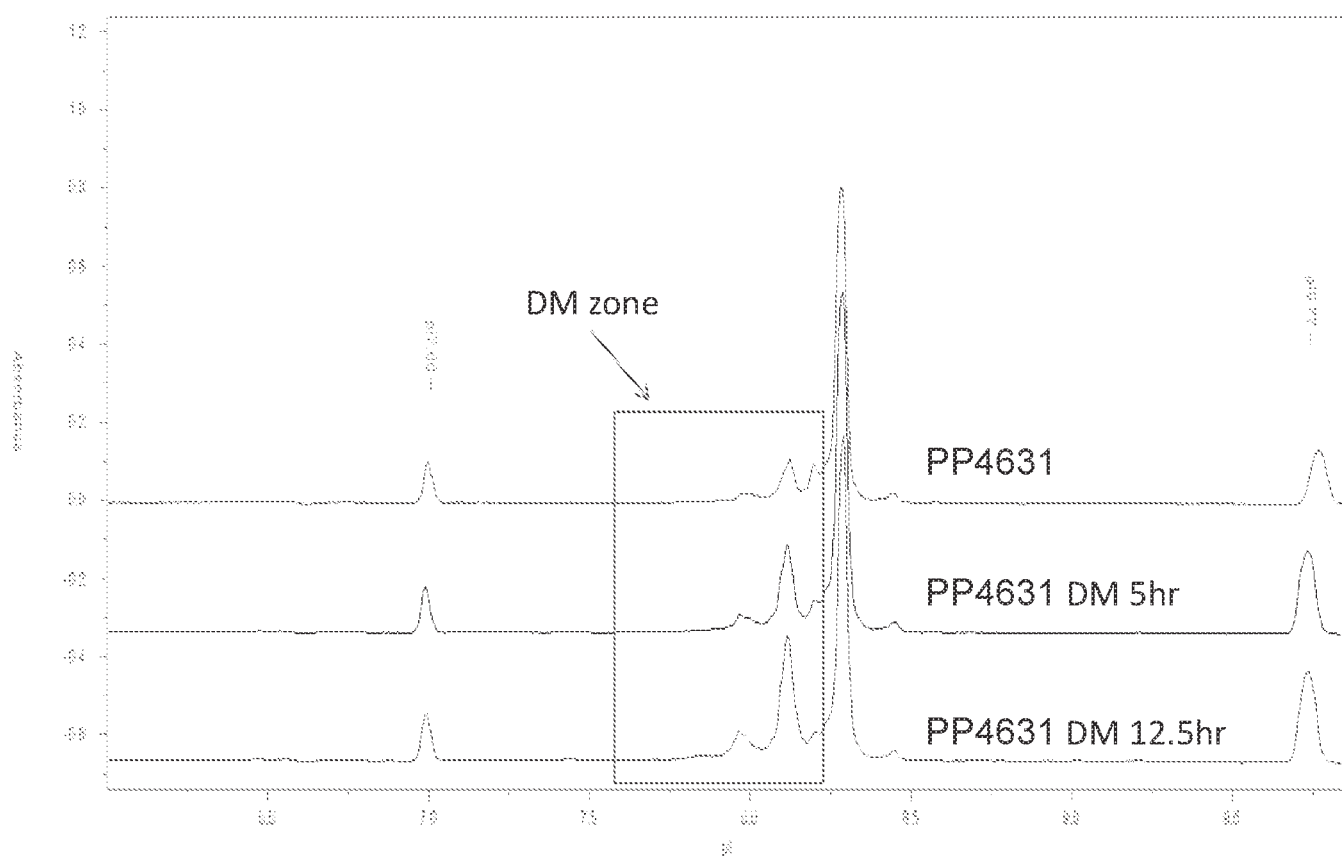


FIG. 53A

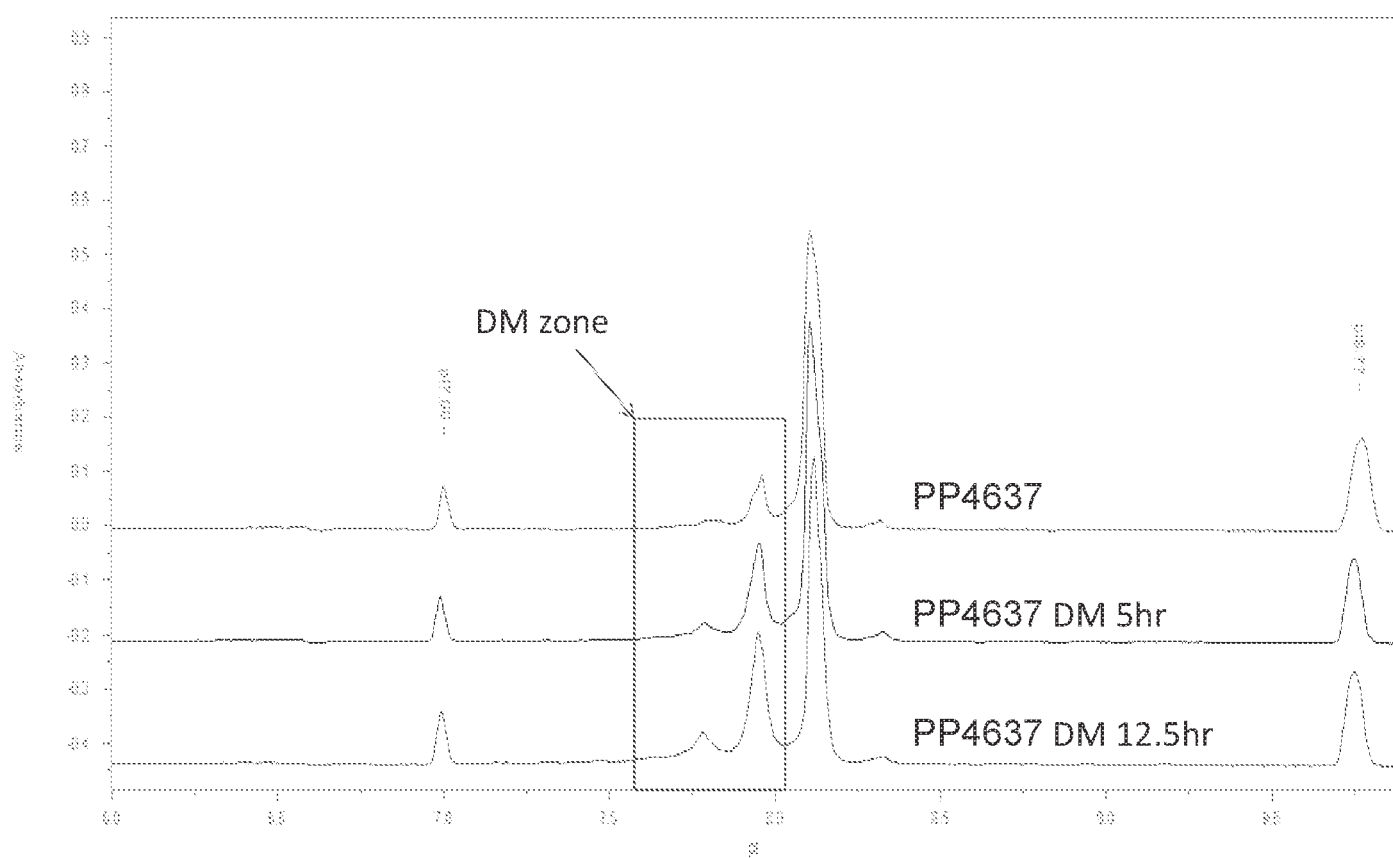


FIG. 53B

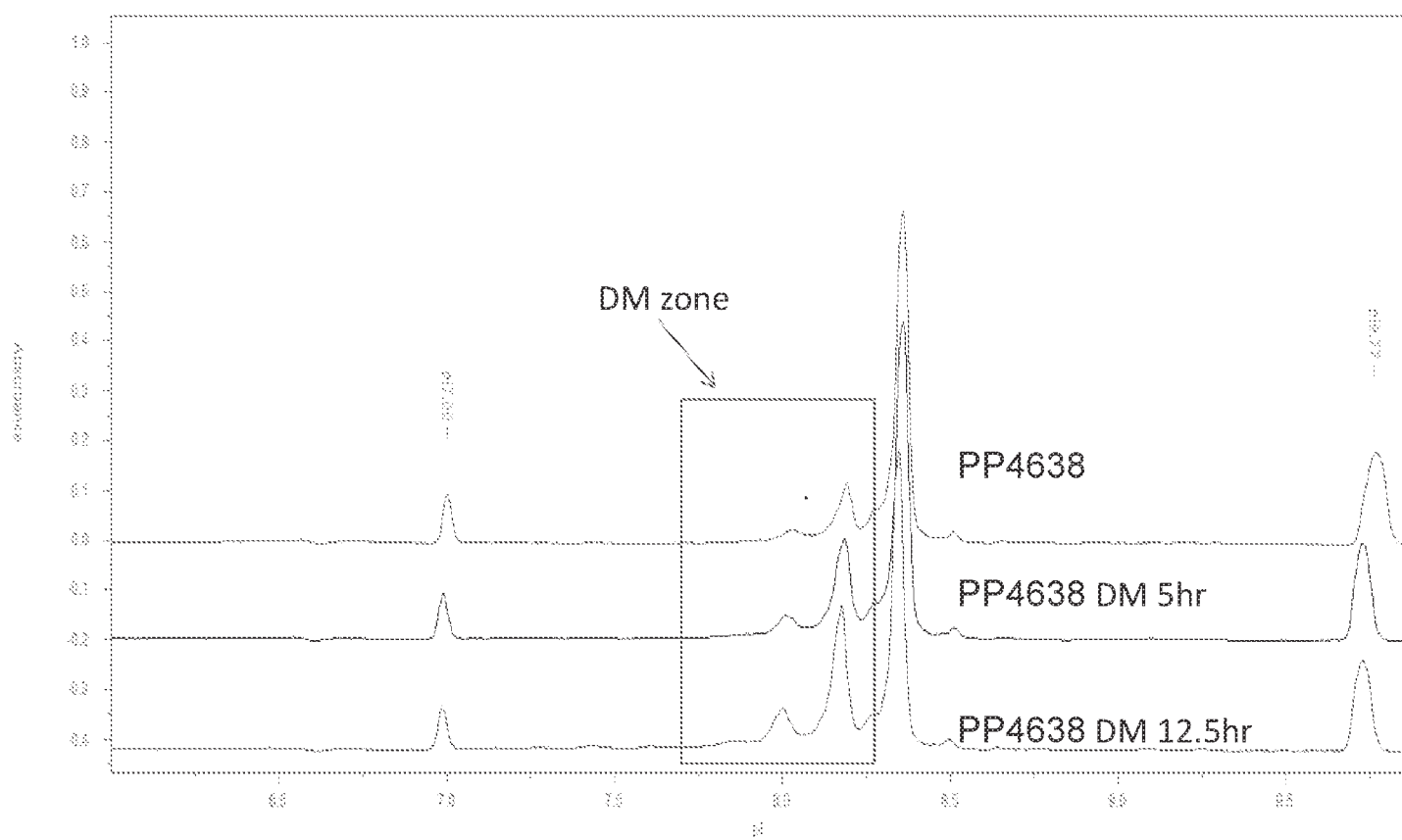
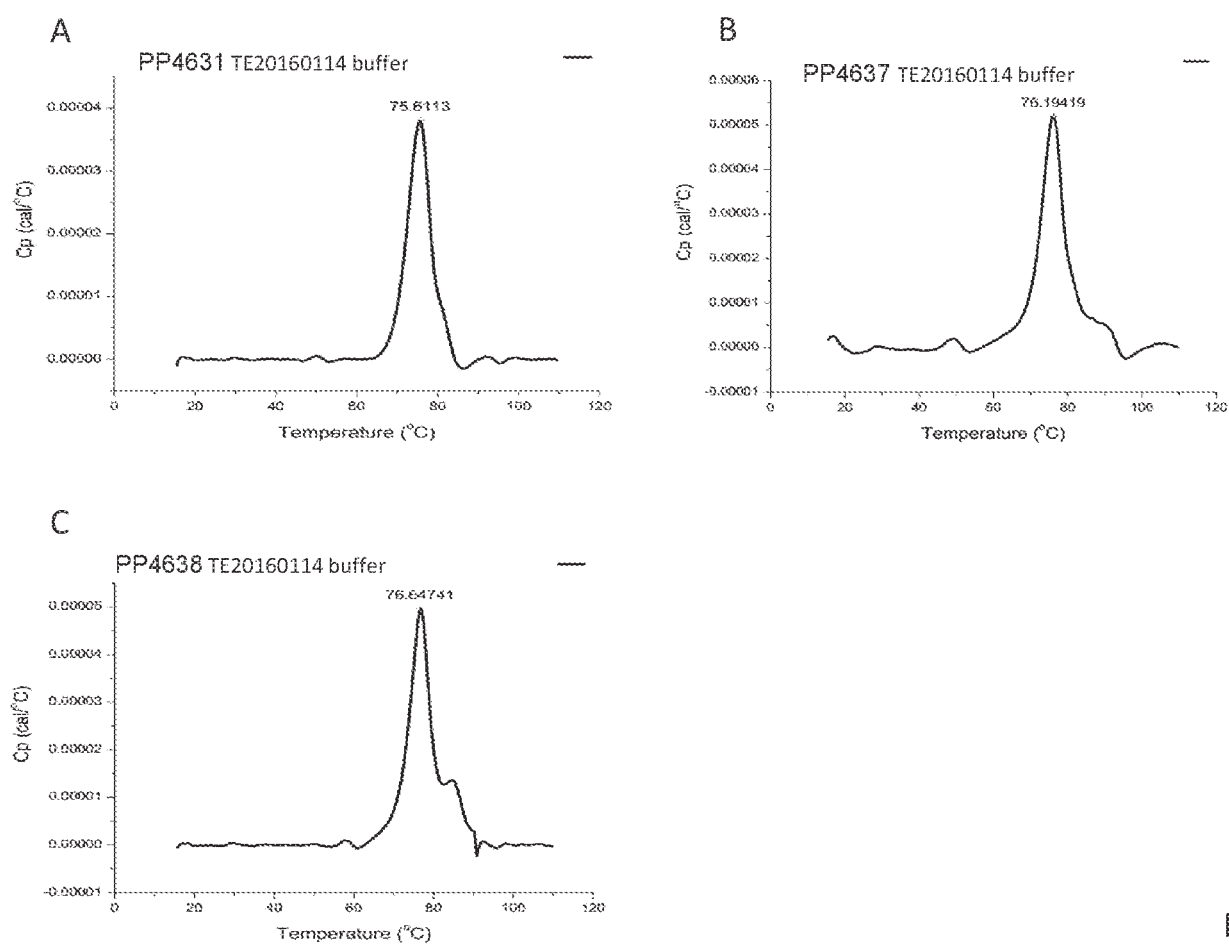


FIG. 53C



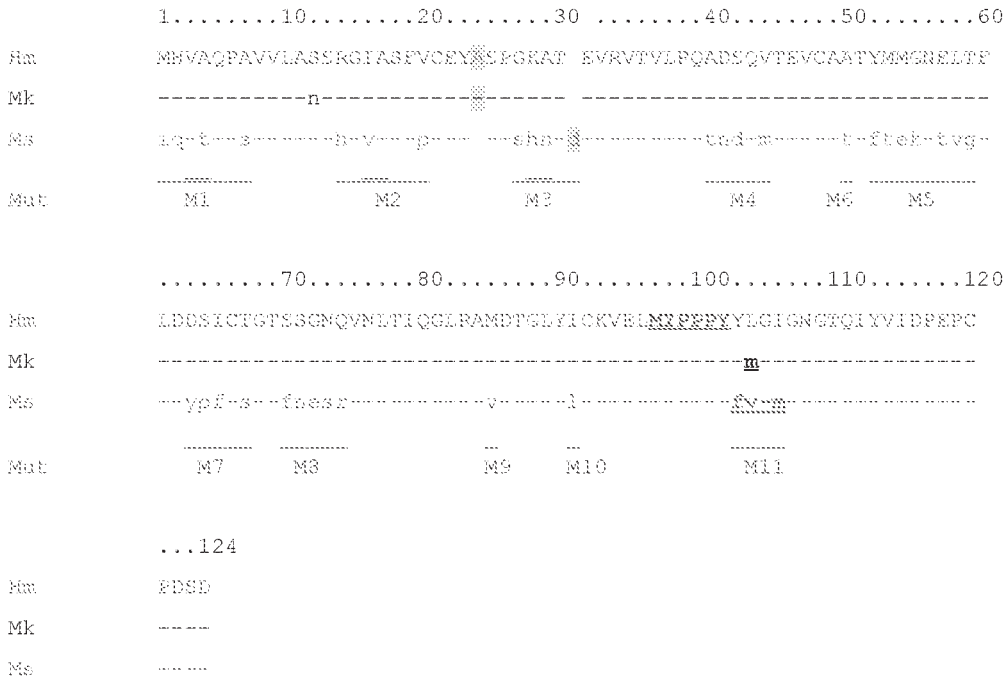


FIG. 55

CTLA-4Fc WT

AMHVAQPAVVLIASSRGIASFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELXXXXXXXXYLGIGNGTQIYVIDPEPCP
 DSDQEPKSSDKTHTSPSPAPPELLGGSSVFLEPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNQGEYCKKVSNAKALPAPIE
 KTISKAKGQPREPOVYTLPPSRDELTKNOVSLTCLVKGFPYPSDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTOKSLSLSPGK

CTLA-4Fc M1

AgvvtgPwVLIASSRGIASFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELXXXXXXXXYLGIGNGTQIYVIDPEPCP
 SDQEPKSSDKTHTSPSPAPPELLGGSSVFLEPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNQGEYCKKVSNAKALPAPIE
 TTISKAKGQPREPOVYTLPPSRDELTKNOVSLTCLVKGFPYPSDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTOKSLSLSPGK

CTLA-4Fc M2

AMHVAQPAVVLIASSRGIASFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELXXXXXXXXYLGIGNGTQIYVIDPEPCP
 DSDQEPKSSDKTHTSPSPAPPELLGGSSVFLEPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNQGEYCKKVSNAKALPAPIE
 KTISKAKGQPREPOVYTLPPSRDELTKNOVSLTCLVKGFPYPSDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTOKSLSLSPGK

CTLA-4Fc M3

AMHVAQPAVVLIASSRGIASFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELXXXXXXXXYLGIGNGTQIYVIDPEPCP
 PDSDQEPKSSDKTHTSPSPAPPELLGGSSVFLEPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNQGEYCKKVSNAKALPAPIE
 EKTISKAKGQPREPOVYTLPPSRDELTKNOVSLTCLVKGFPYPSDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTOKSLSLSPGK

CTLA-4Fc M4

AMHVAQPAVVLIASSRGIASFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELXXXXXXXXYLGIGNGTQIYVIDPEPCP
 DSDQEPKSSDKTHTSPSPAPPELLGGSSVFLEPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNQGEYCKKVSNAKALPAPIE
 KTISKAKGQPREPOVYTLPPSRDELTKNOVSLTCLVKGFPYPSDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTOKSLSLSPGK

CTLA-4Fc M5

AMHVAQPAVVLIASSRGIASFVCEYASPGKATEVRVTVLRQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELXXXXXXXXYLGIGNGTQIYVIDPEPCP
 DSDQEPKSSDKTHTSPSPAPPELLGGSSVFLEPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHODWLNQGEYCKKVSNAKALPAPIE
 KTISKAKGQPREPOVYTLPPSRDELTKNOVSLTCLVKGFPYPSDIAVEWESNGOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTOKSLSLSPGK

FIG. 56A

[illegible]

FIG. 56B

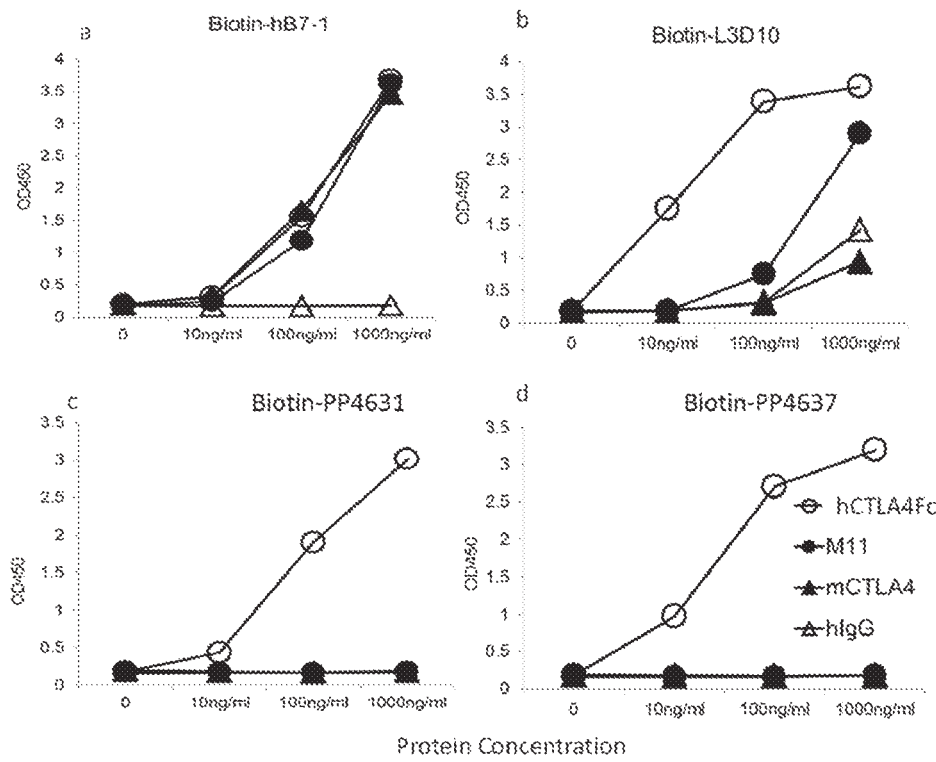


FIG. 57

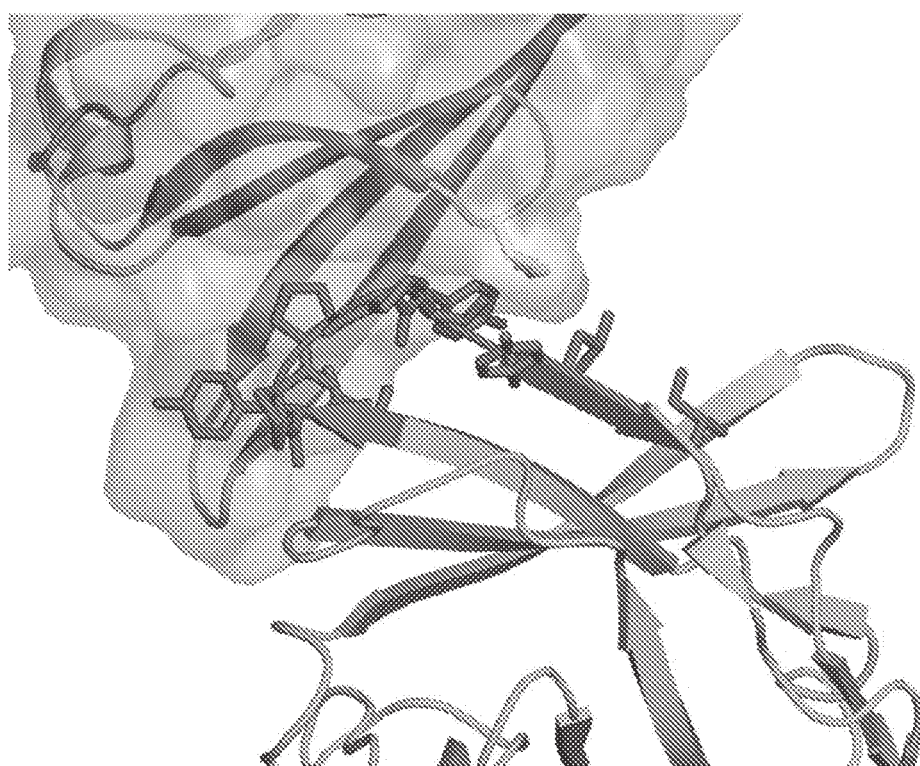


FIG. 58

CTLA-4Fc WT

AMHVAQPAVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYLGIGNGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

CTLA-4Fc M12

AgvvtqPpVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATFteknctvgFLDDSICTGTfnesrVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYfvgGNGGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

CTLA-4Fc M13

MHVAQPAVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYfvgGNGGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

CTLA-4Fc M14

AgvvtqPpVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATFteknctvgFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYfvgGNGGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

CTLA-4Fc M15

MHVAQPAVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYfvgGNGGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

CTLA-4Fc M16

AgvvtqPpVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATFteknctvgFLDDSICTGTfnesrVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYfvgGNGGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

CTLA-4Fc M17

MHVAQPAVVLASSRGIASFVCEYASPGKATEVVRVTVLRLQADSQVTEVCAATYMMGNELTFLDDSICTGTSSGNQVNLTIQGLRAMDTGLYICKVELNXXXXXXXXYfvgGNGGTQIYVIDPEPCPD
SDQEPKSSDKTHTSPSPAPPELLGGSSVFLPPPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFPSCVMHEALHNHYTQKSLSLSPGK

FIG. 59

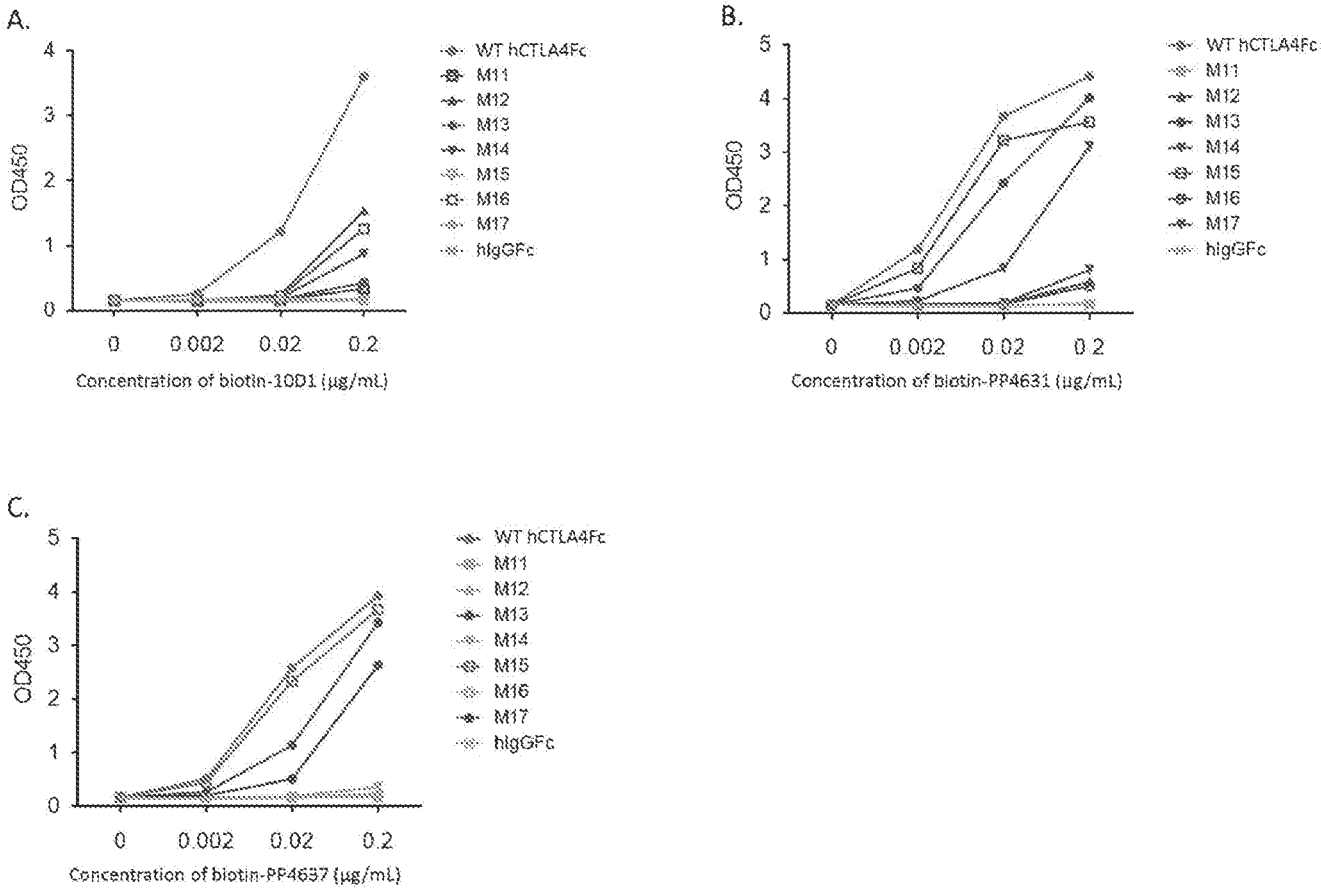


FIG. 60

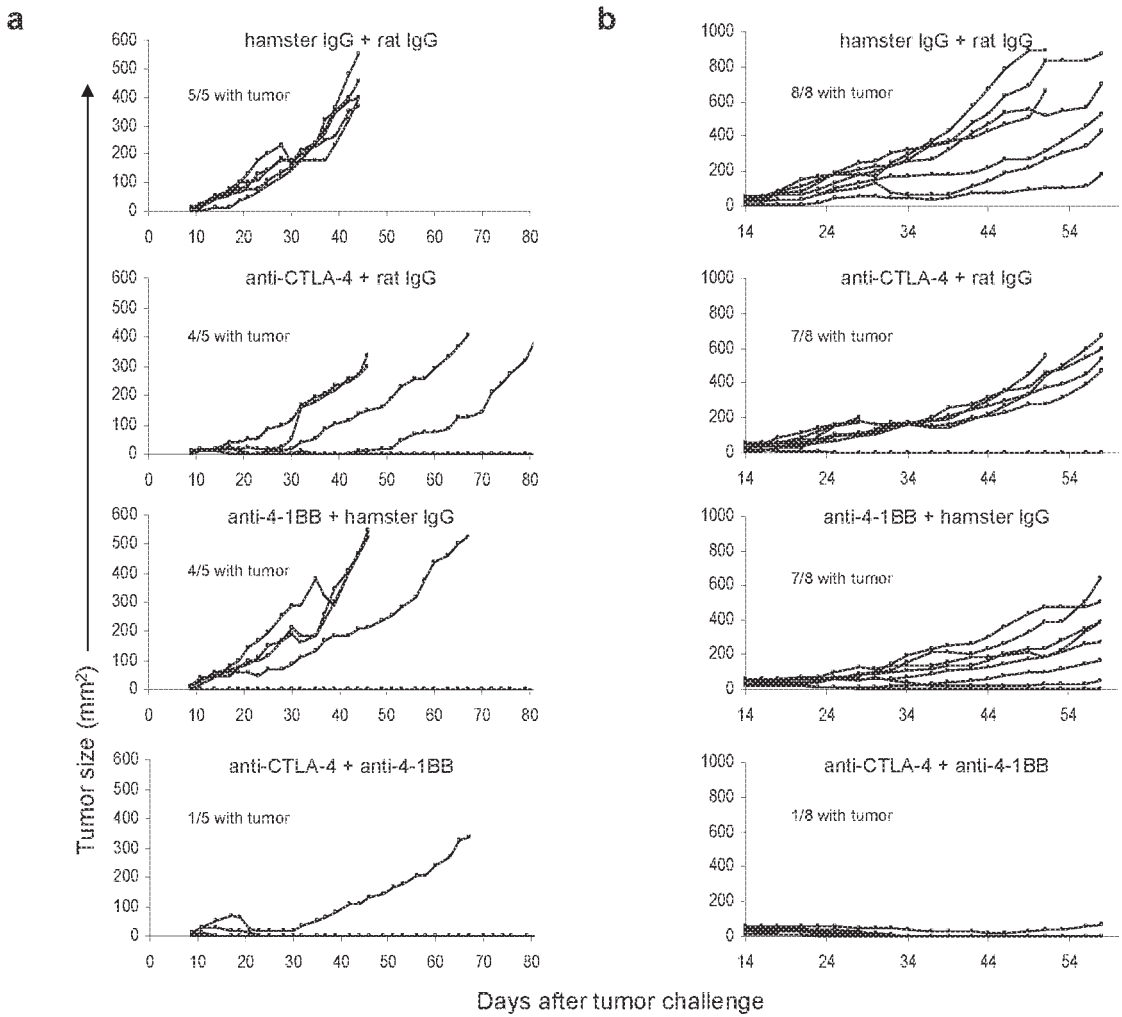


FIG. 61

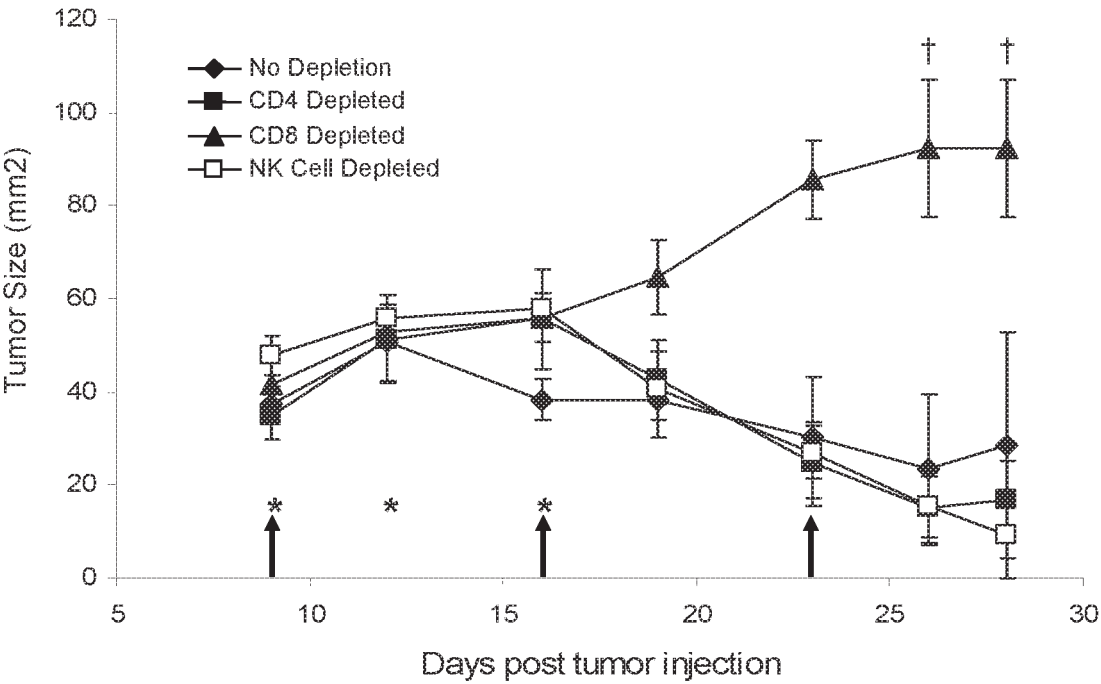


FIG. 62

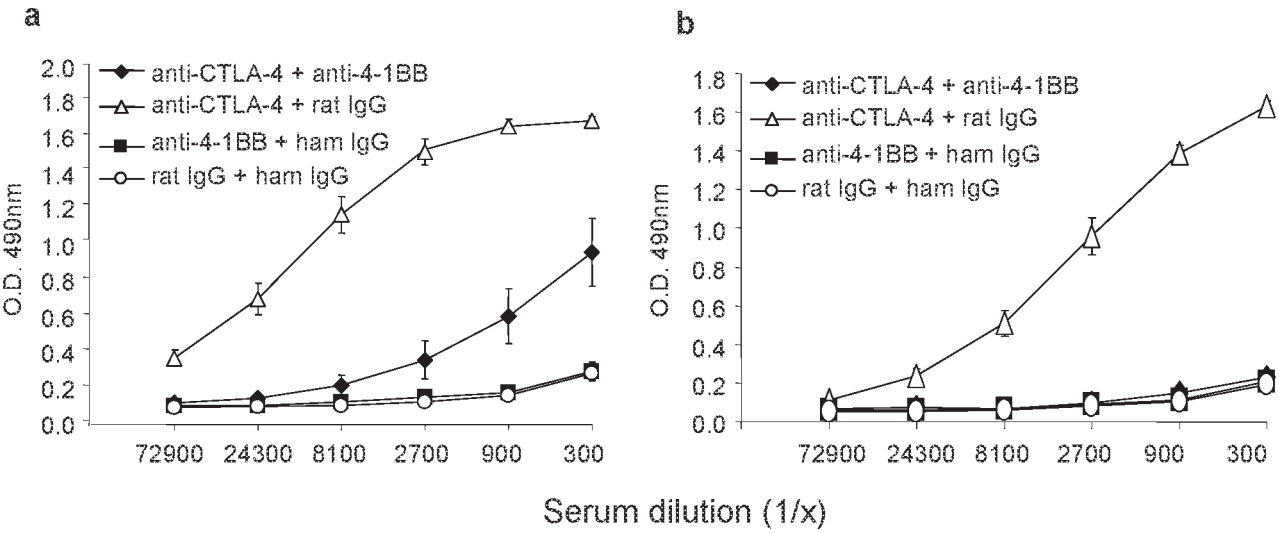


FIG. 63

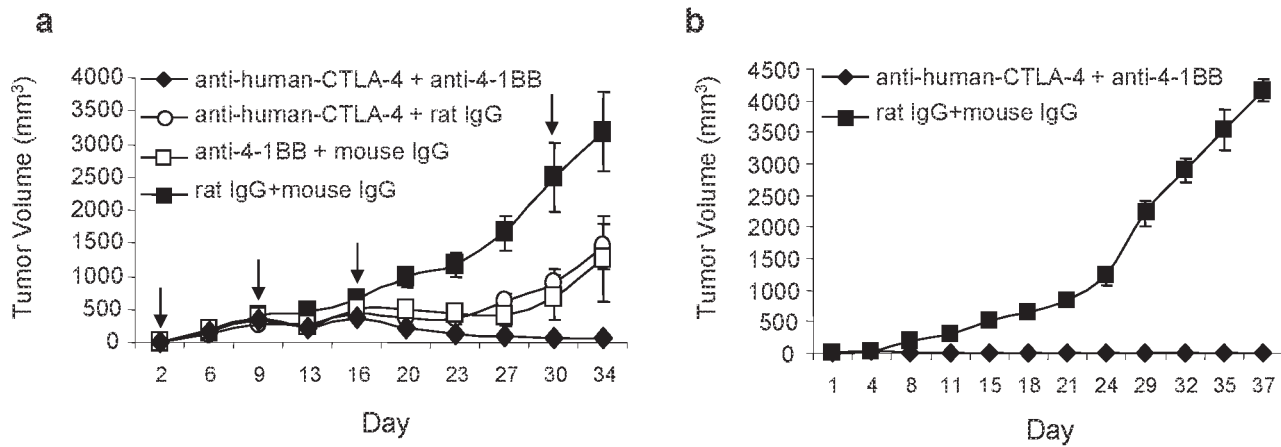


FIG. 64