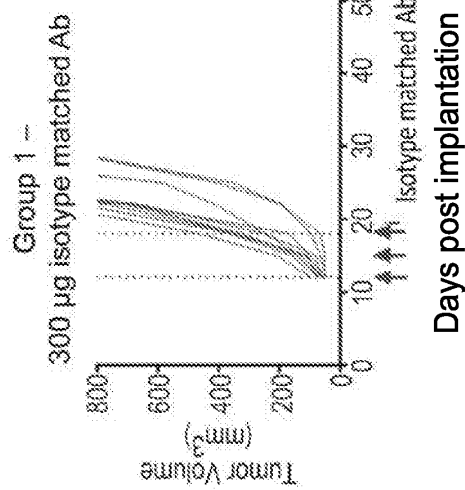


Fig. 1A



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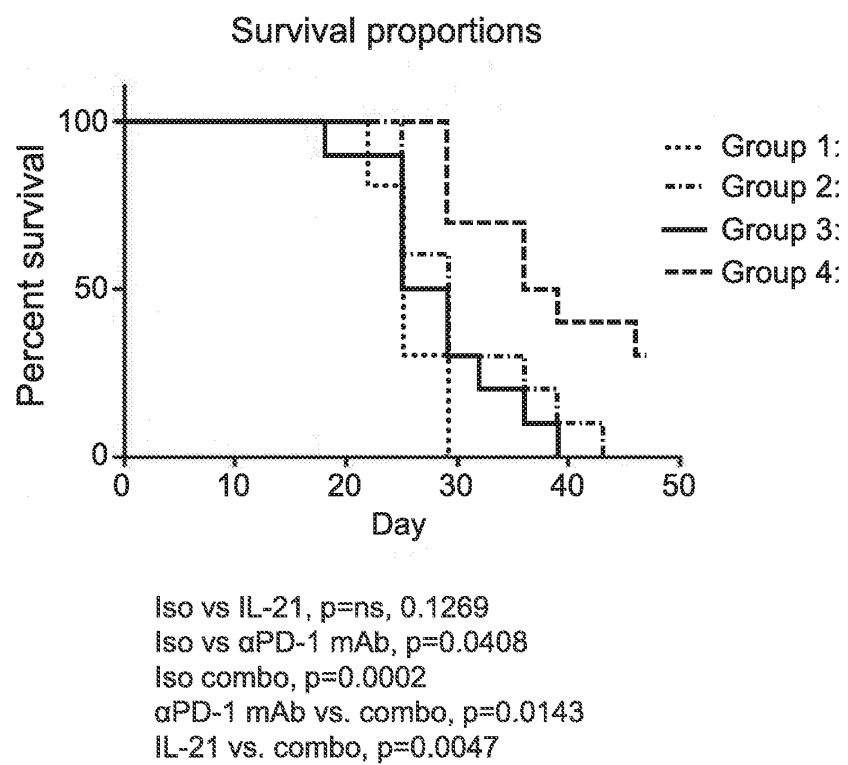
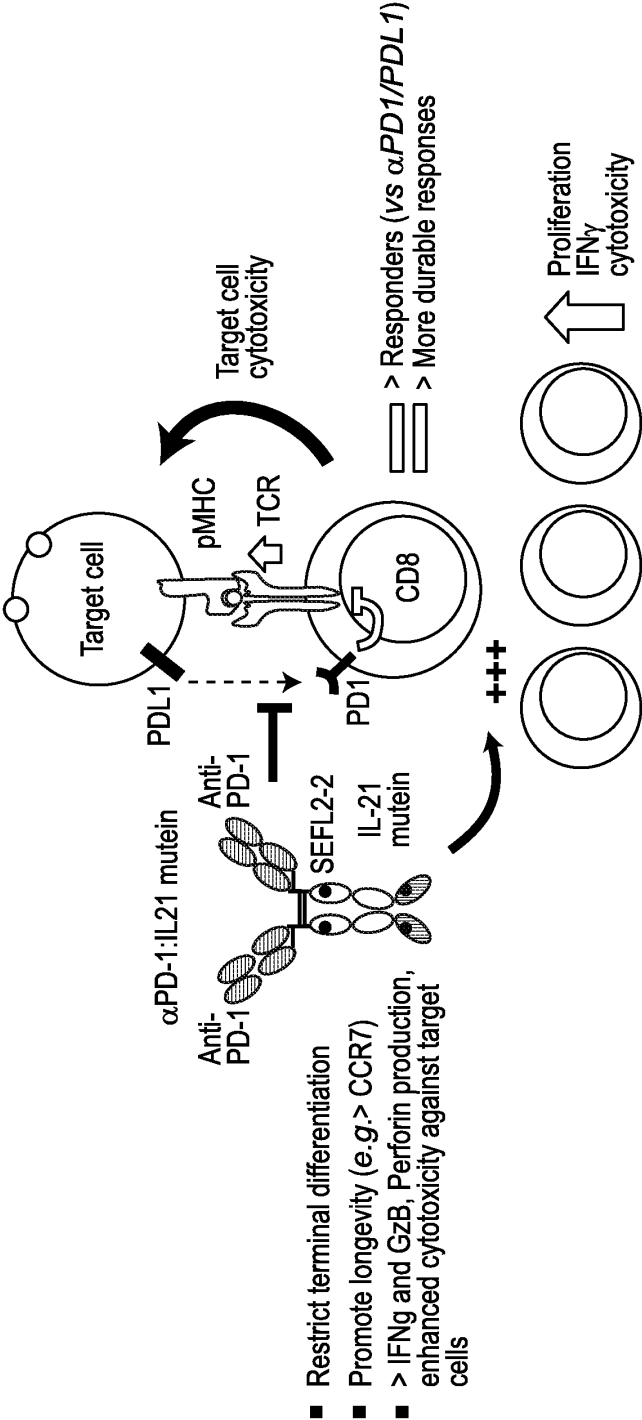
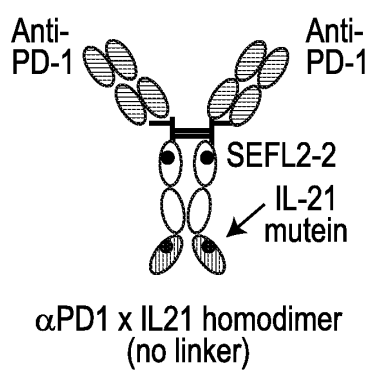
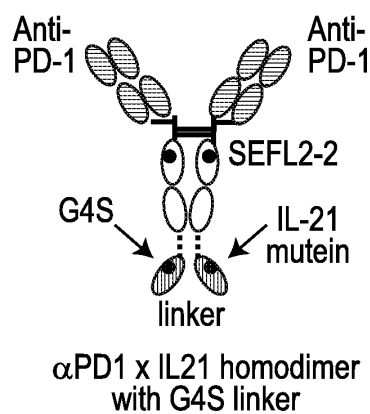
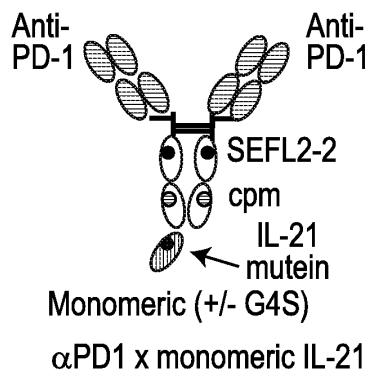
**Fig. 2**

Fig. 3



**Fig. 4A****Fig. 4B****Fig. 4C**

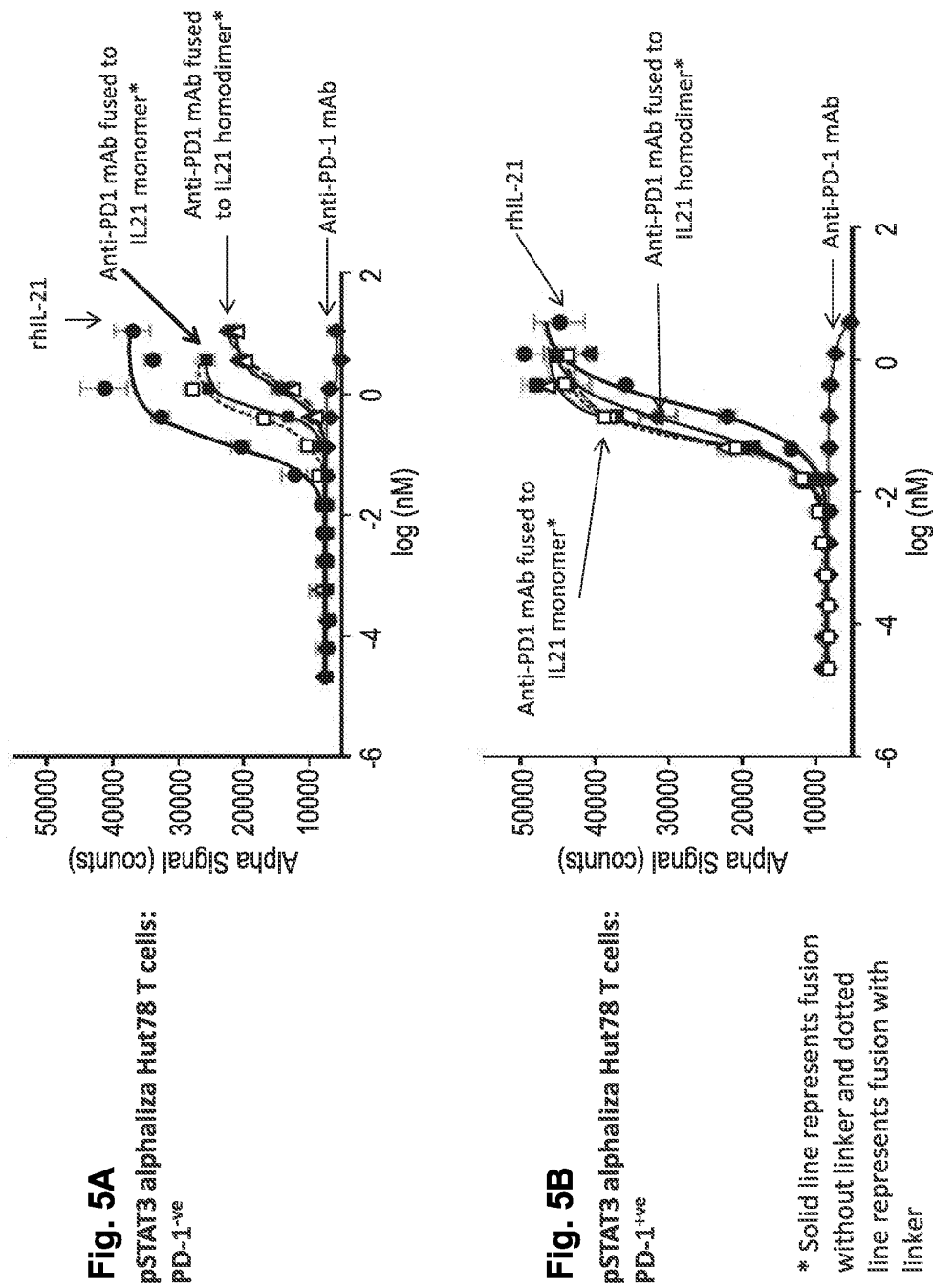
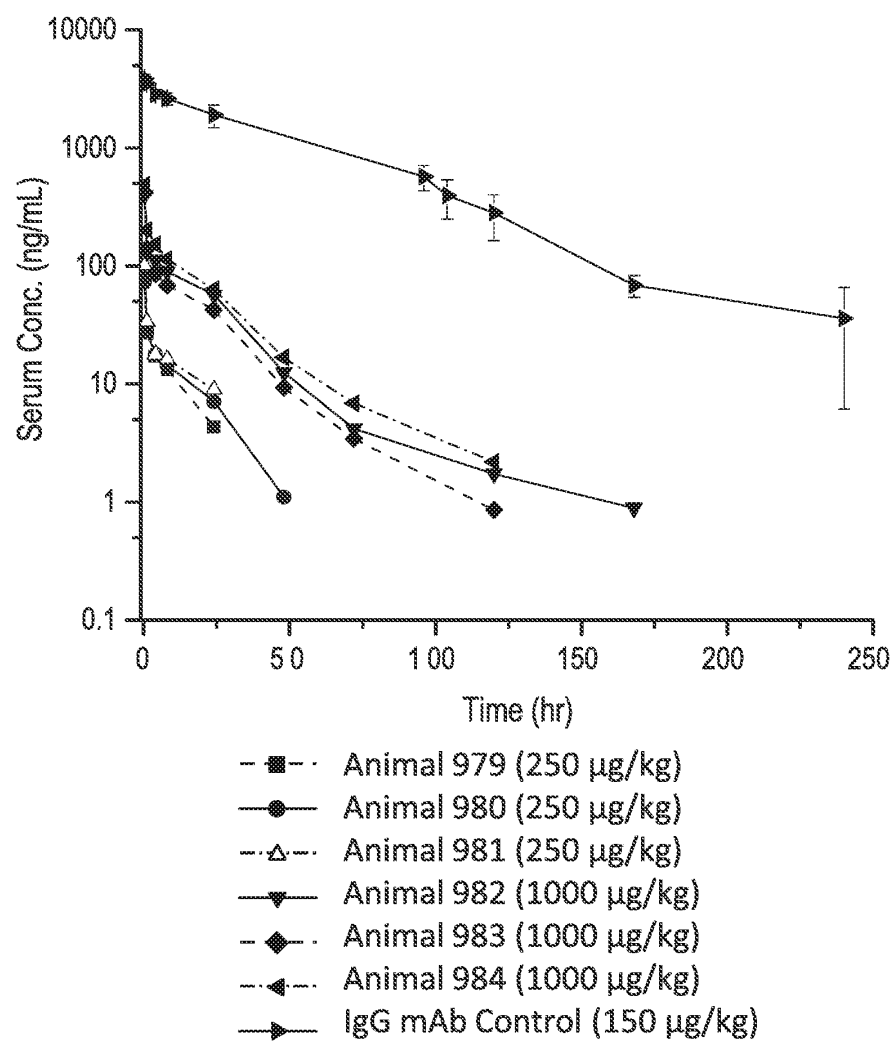


Fig. 5

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**Fig. 6**

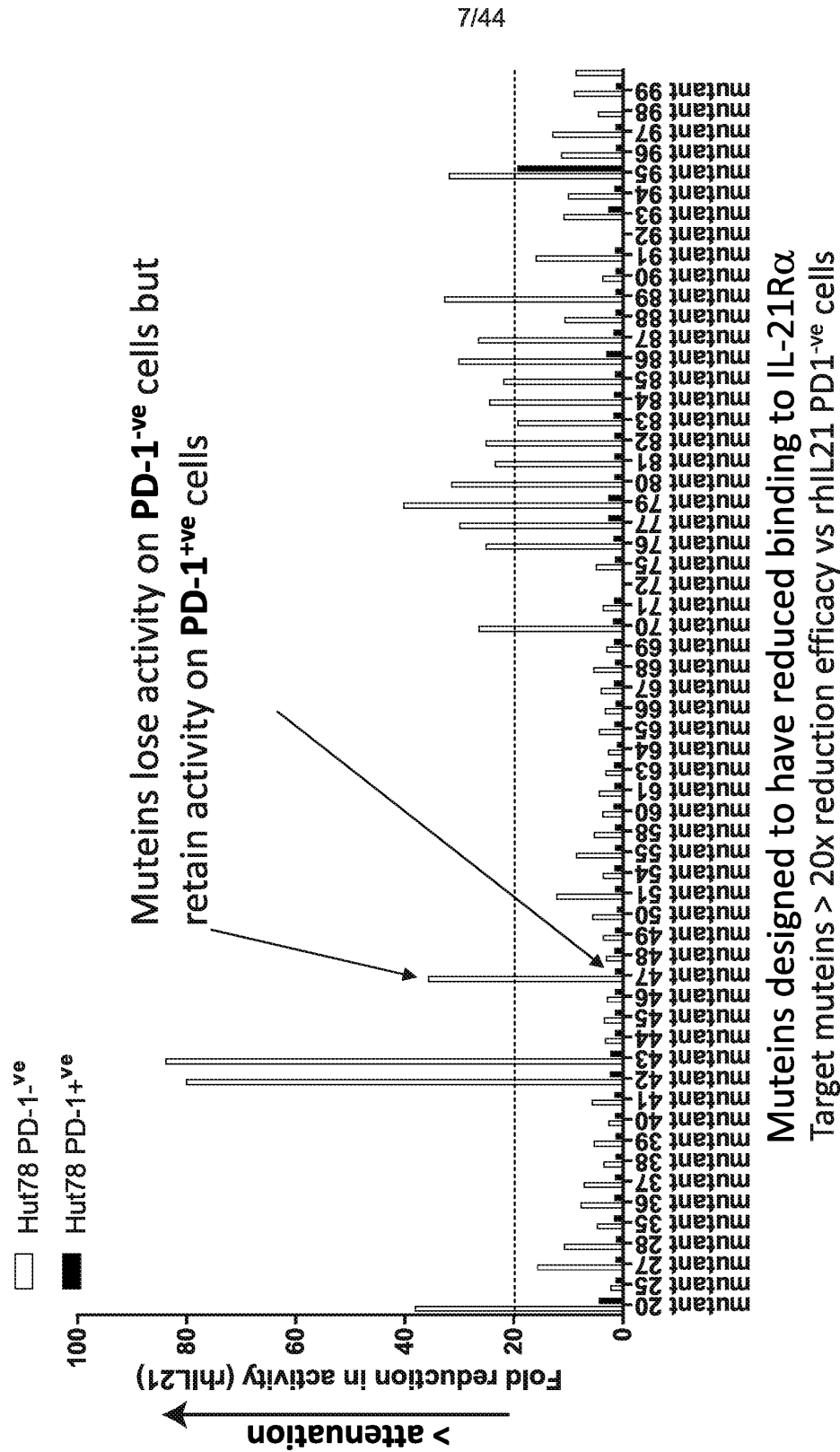


Fig. 7

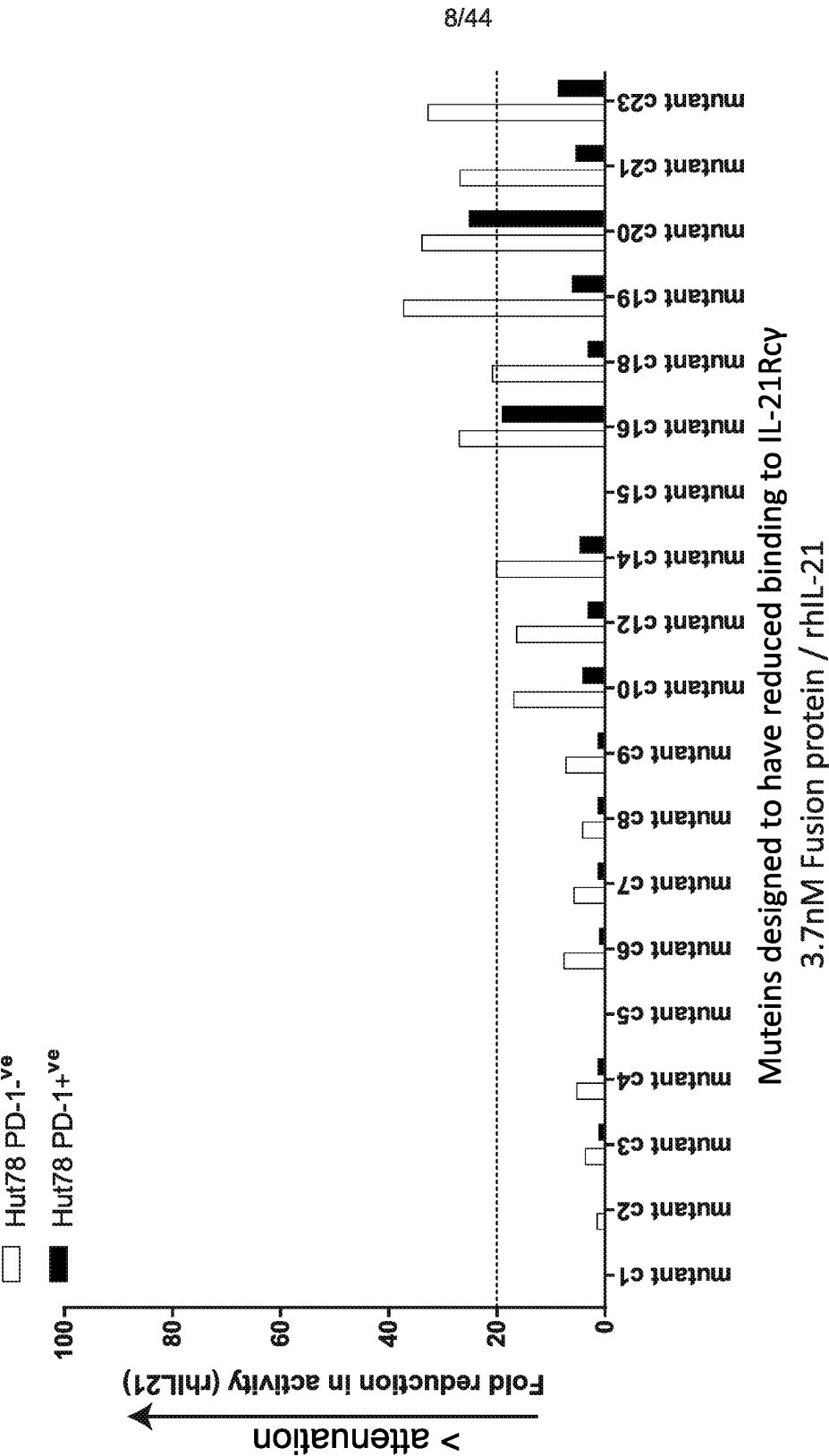


Fig. 8

Identification of muteins which meet criteria (>20 fold attenuation on PD-1^{-ve} cells)
& are dependent on PD-1 for targeting

- Human IL-21
- PD1 mAb
- PD1 mAb x WT IL-21 (mono)
-▲..... PD1mAb x IL-21 mutant 51

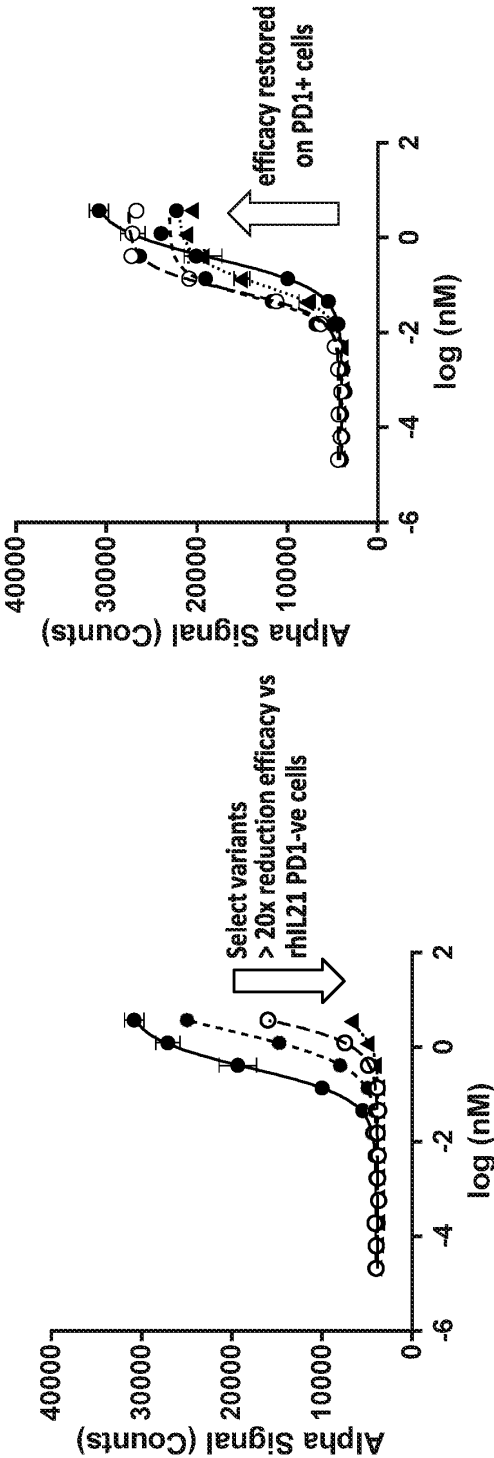
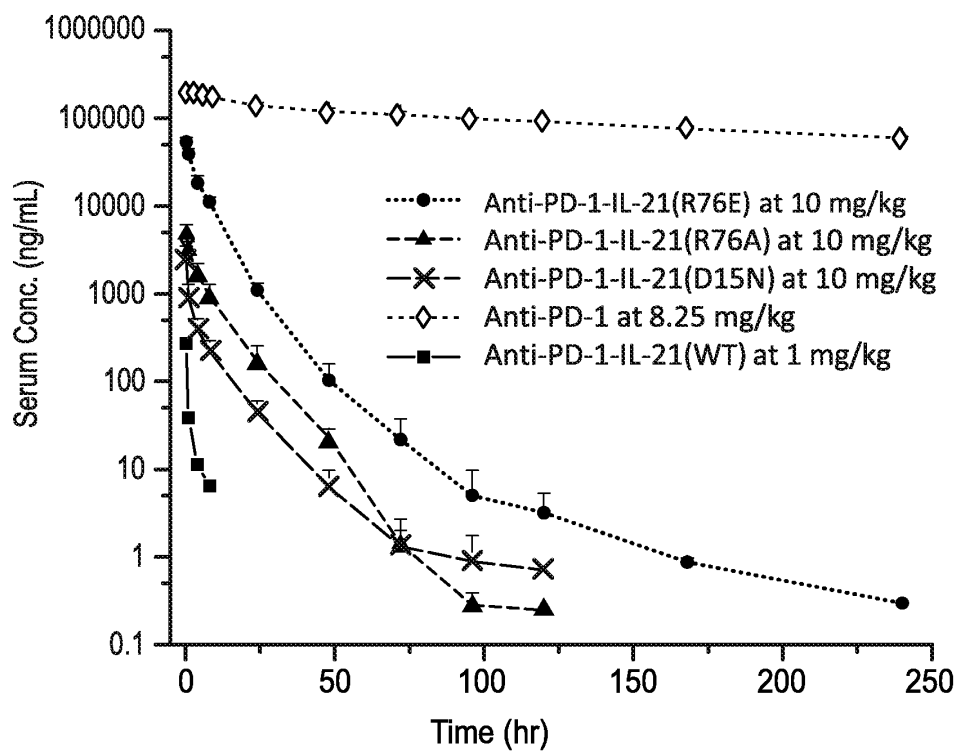


Fig. 9B
PD1^{+ve}

Fig. 9A
PD1^{-ve}

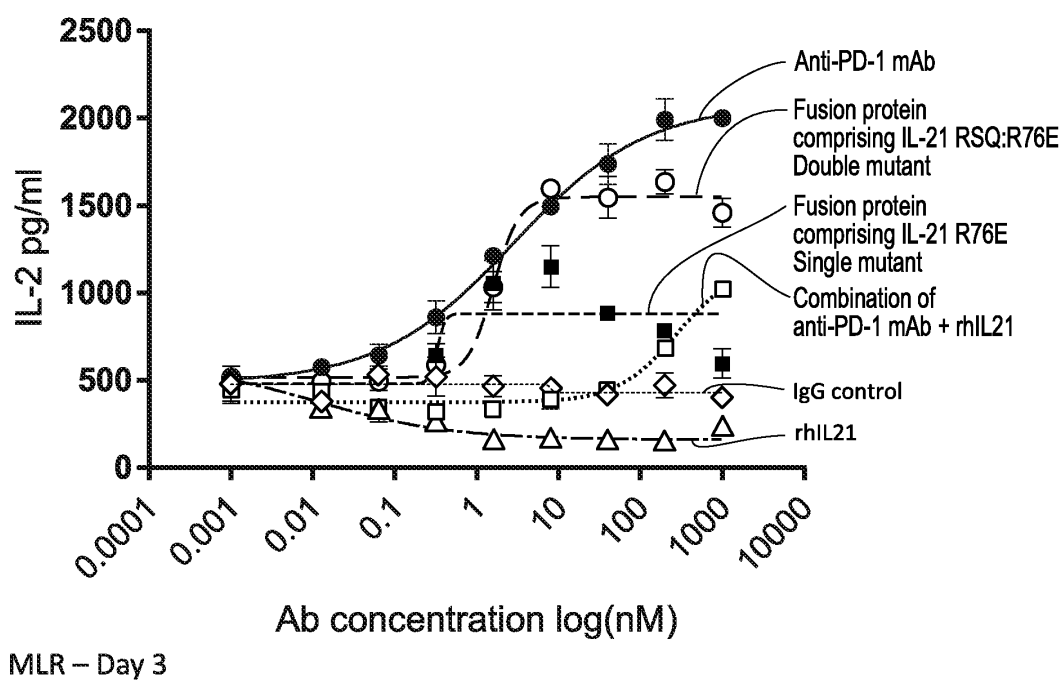
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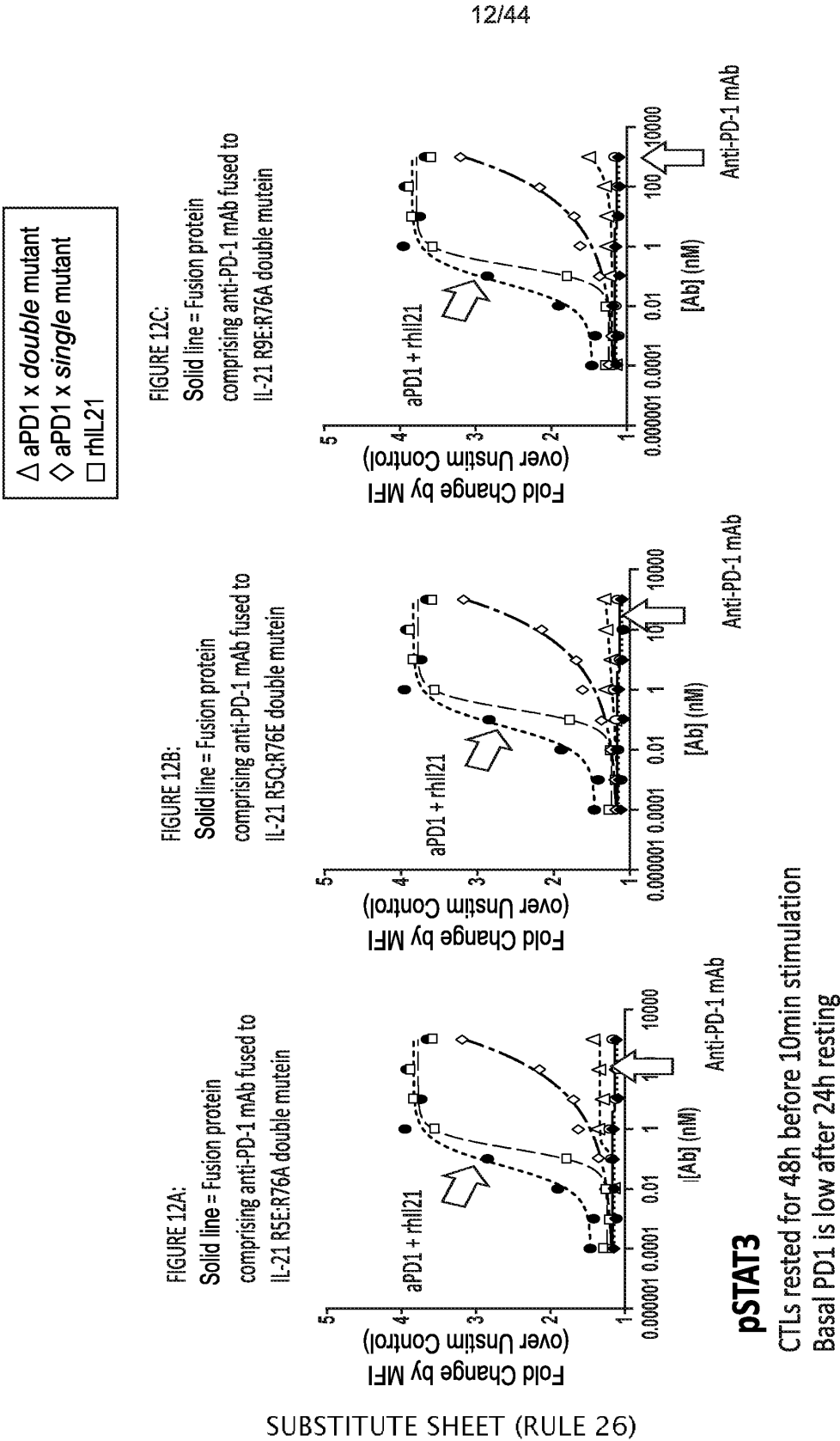


Anti-PD-1 mAb-IL-21 mutein fusion proteins exhibited altered distribution compared to parent anti-PD-1 mAb

Fig. 10

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**Fig. 11**



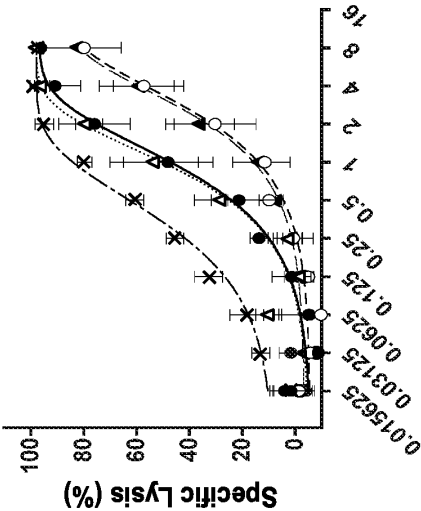
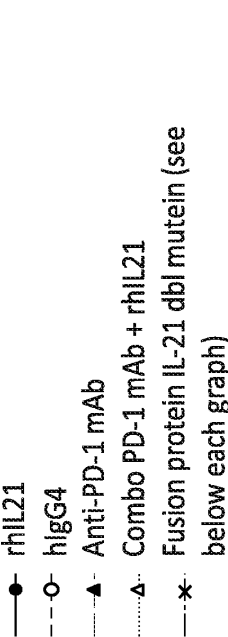


Fig. 13A
Double mutein = IL-21
R5E/R76A

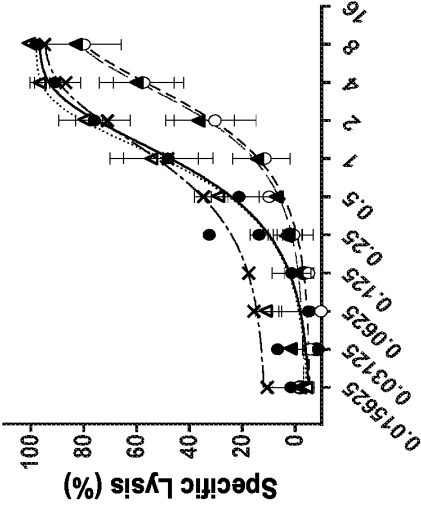


Fig. 13B
Double mutein = IL-21
R5Q/R76E

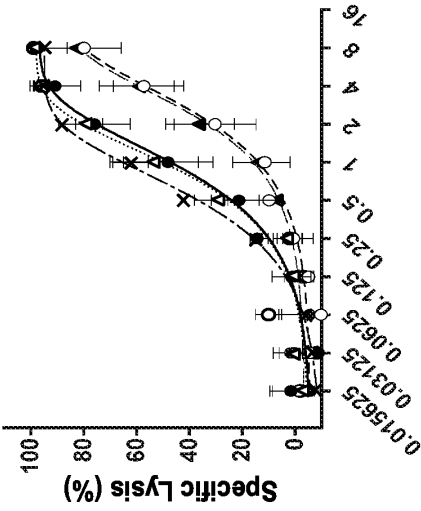
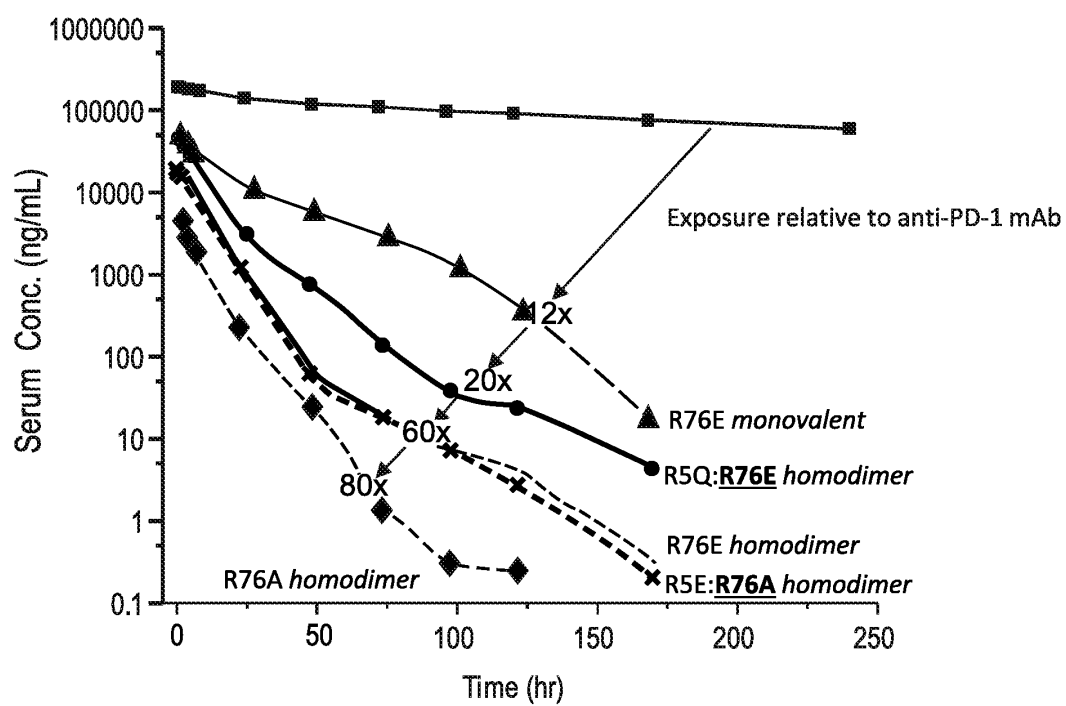
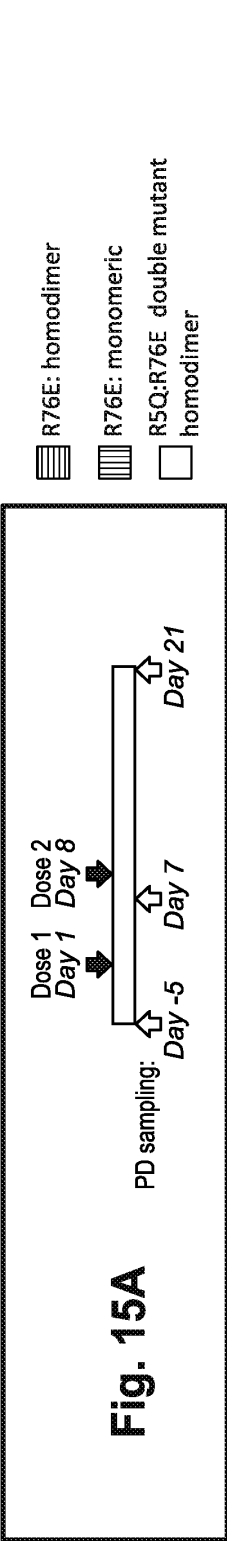


Fig. 13C
Double mutein = IL-21
R9E/R76A

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**Fig. 14**



Day 7 (measurement post-single dose) **Day 21 (measurement 14 days post-repeat dose)**

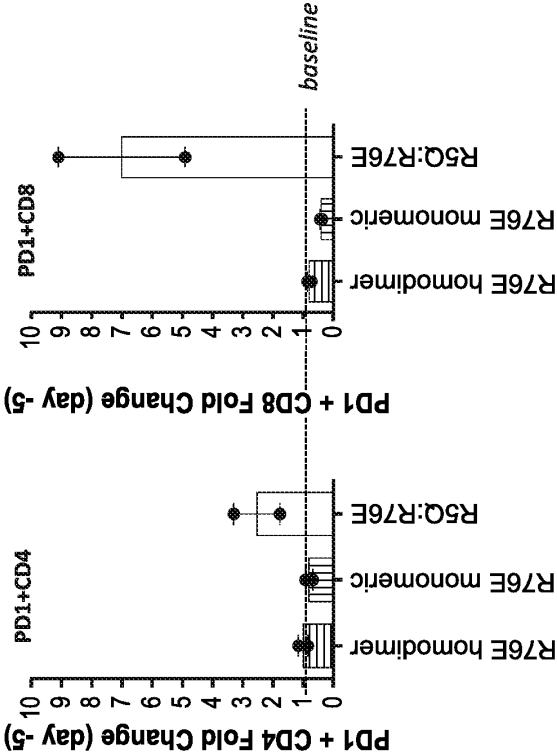
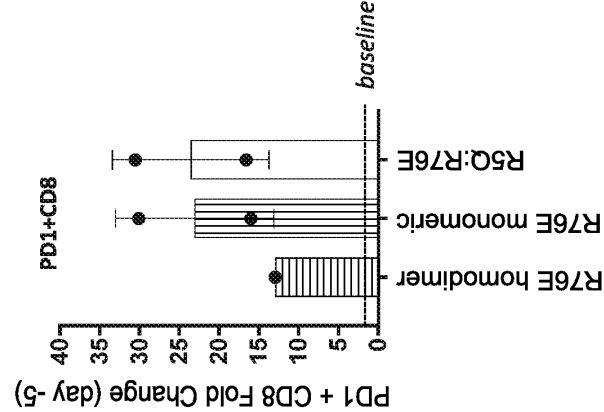


Fig. 15C



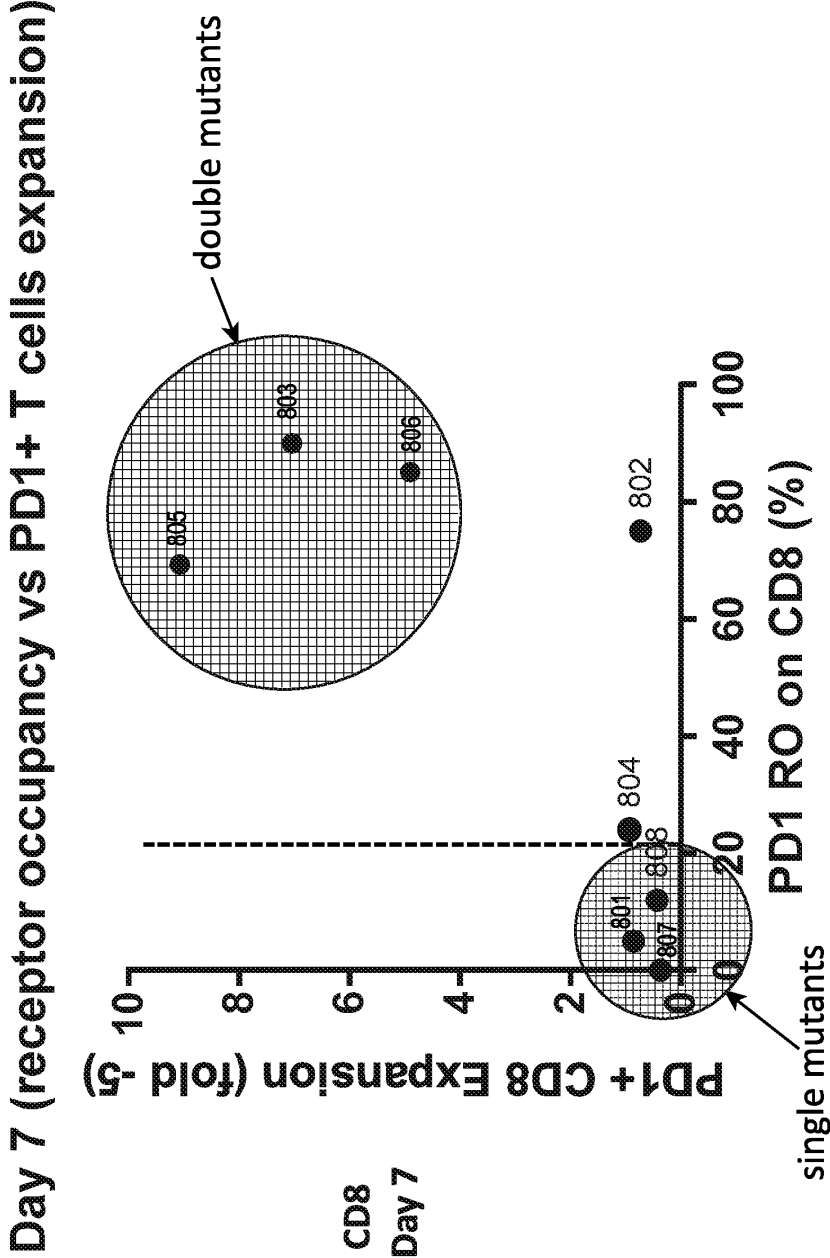


Fig. 16

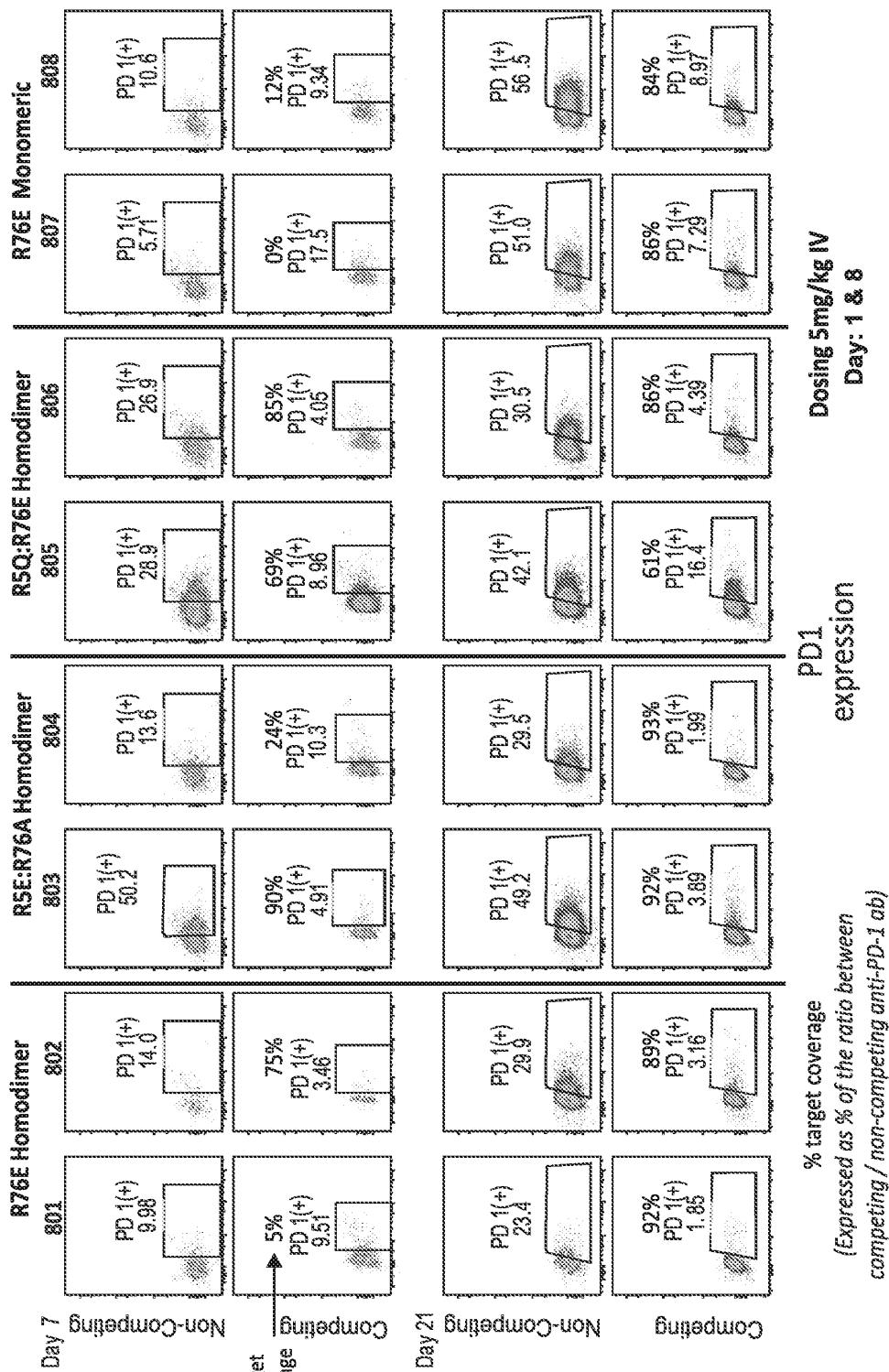


Fig. 17

PD-1 targeting needed for pSTAT3 signal, activity of mutein similar
across different PD-1 mAb variants

R9E, R76A HUT78

R9E, R76A HUT78-PD1

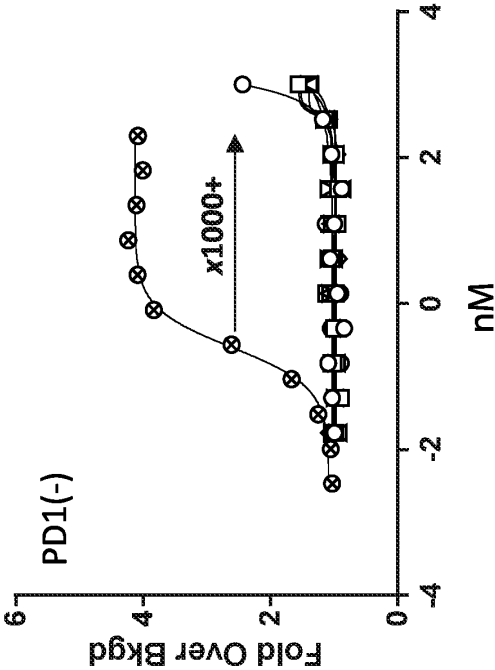


Fig. 18A

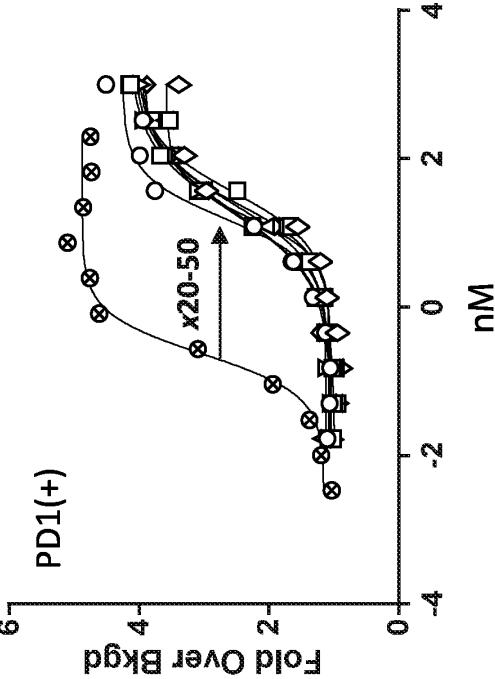
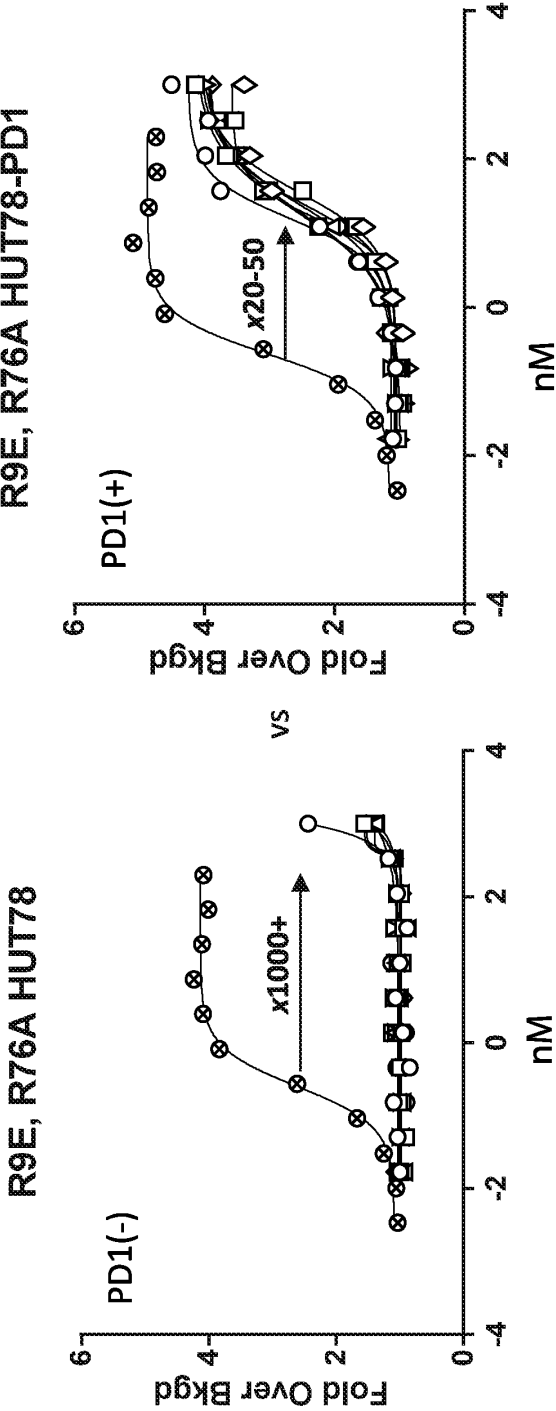


Fig. 18B

PD-1 targeting needed for pSTAT3 signal, activity of mutein similar across different PD-1 mAb variants



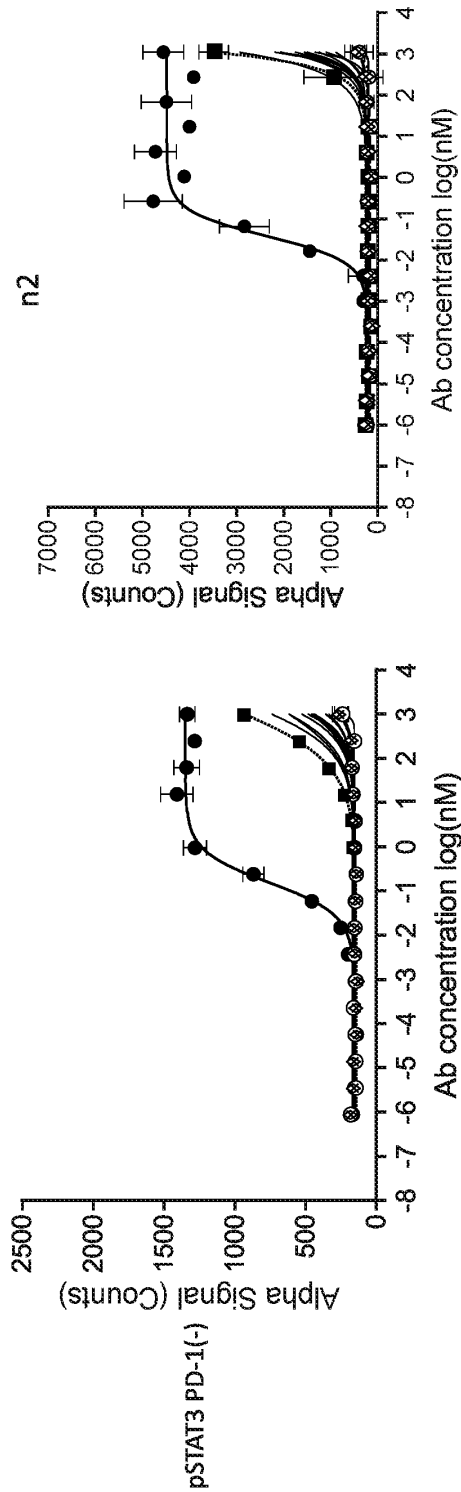
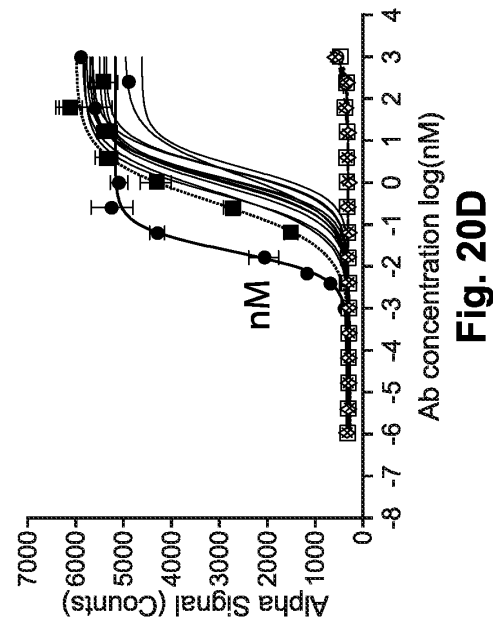
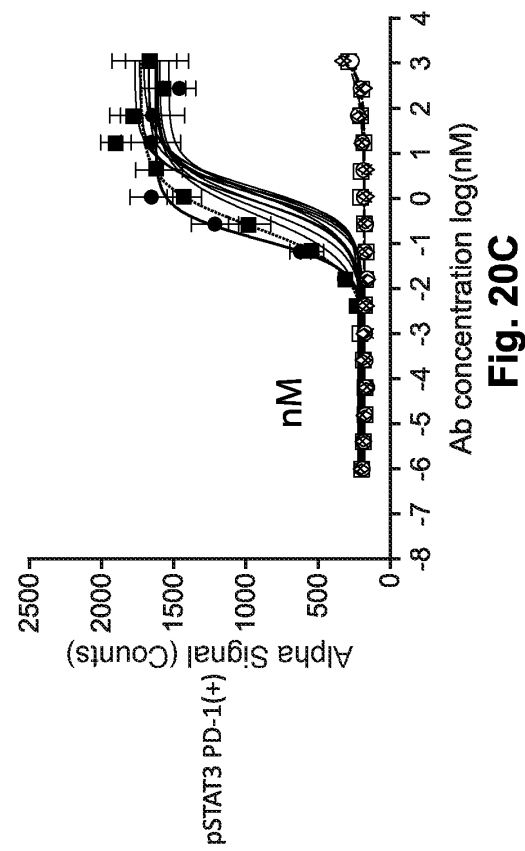
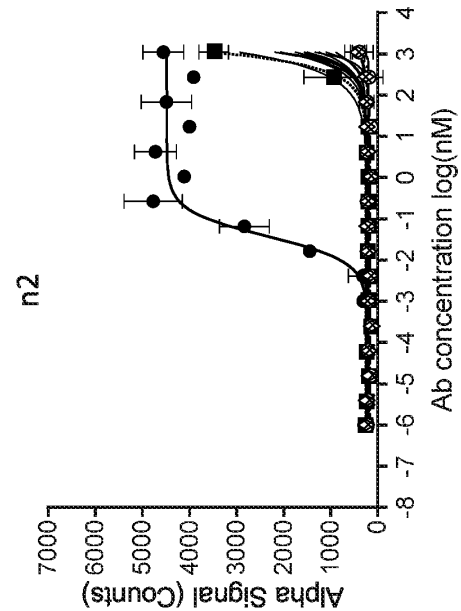
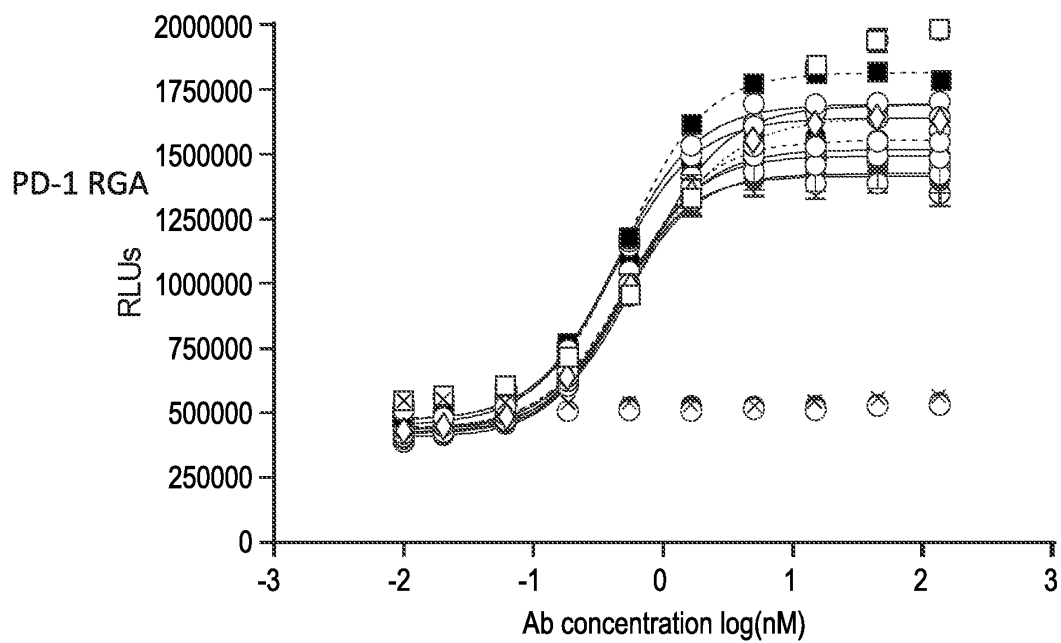
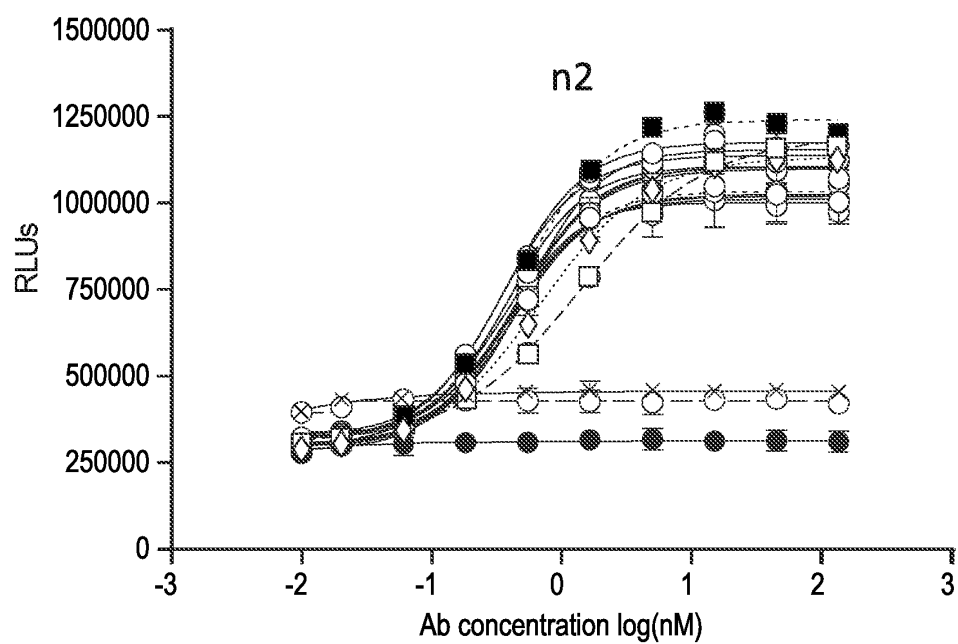


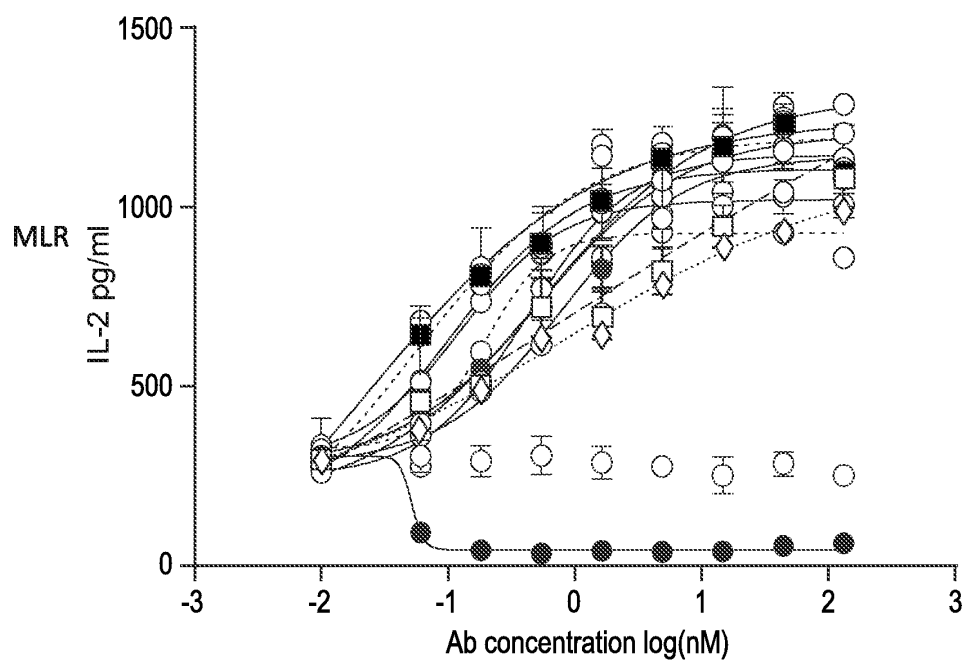
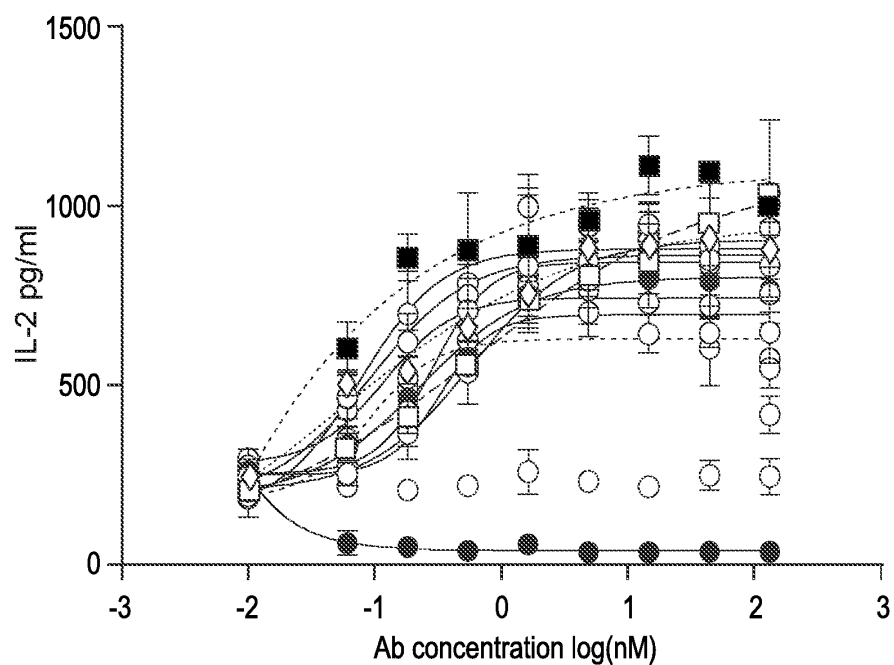
Fig. 20B

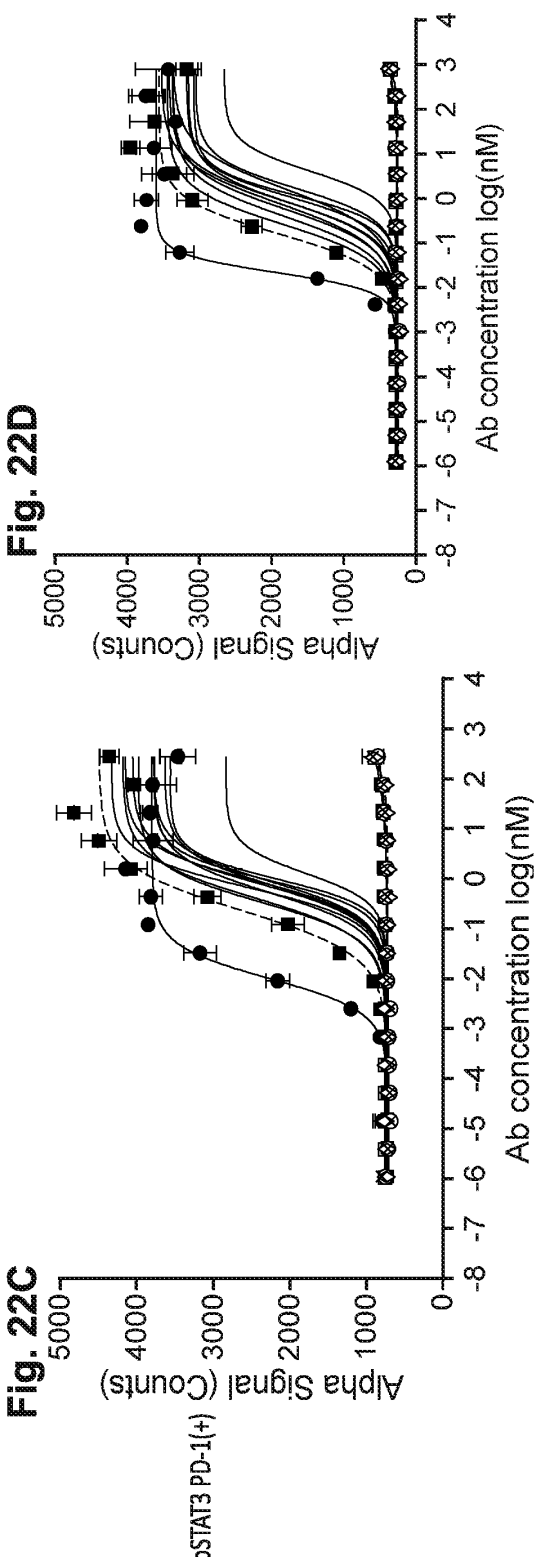
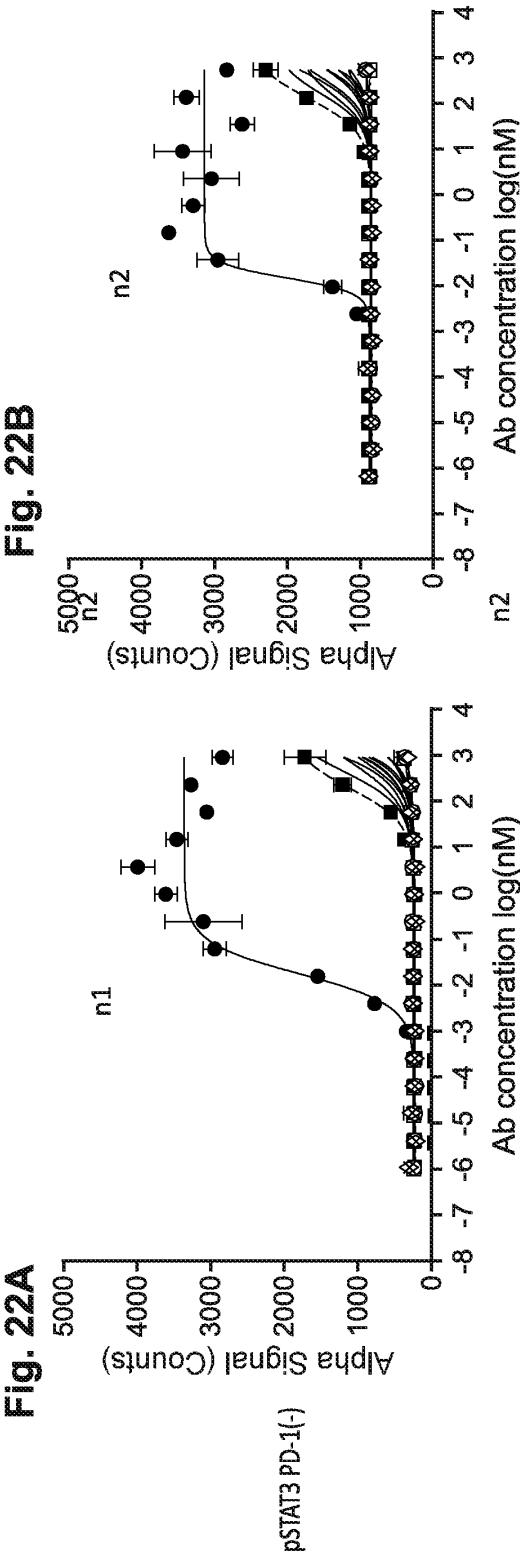


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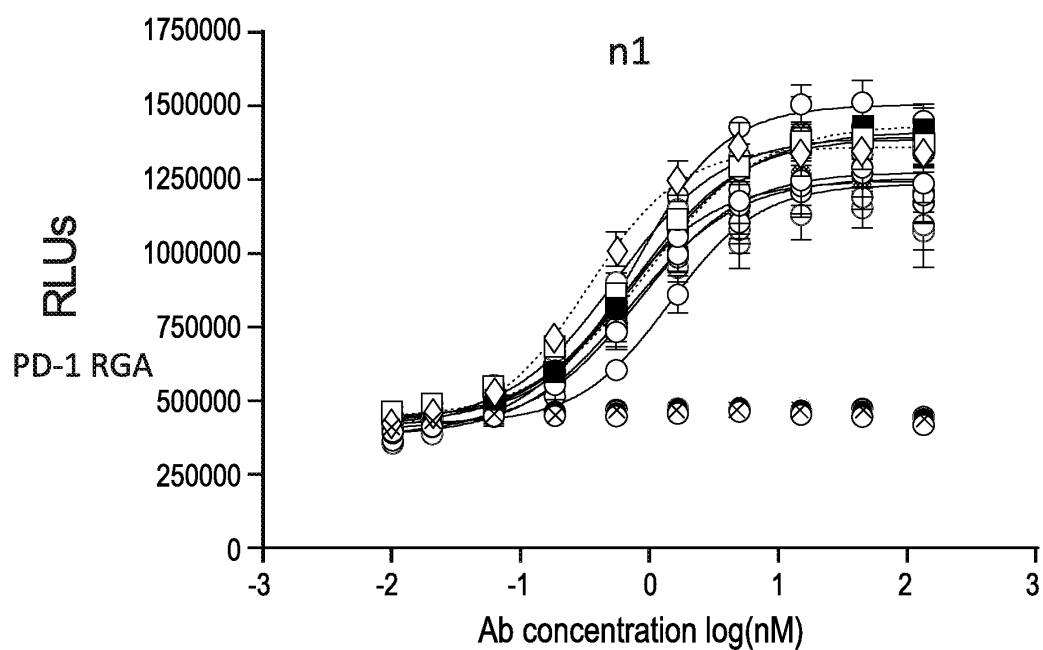
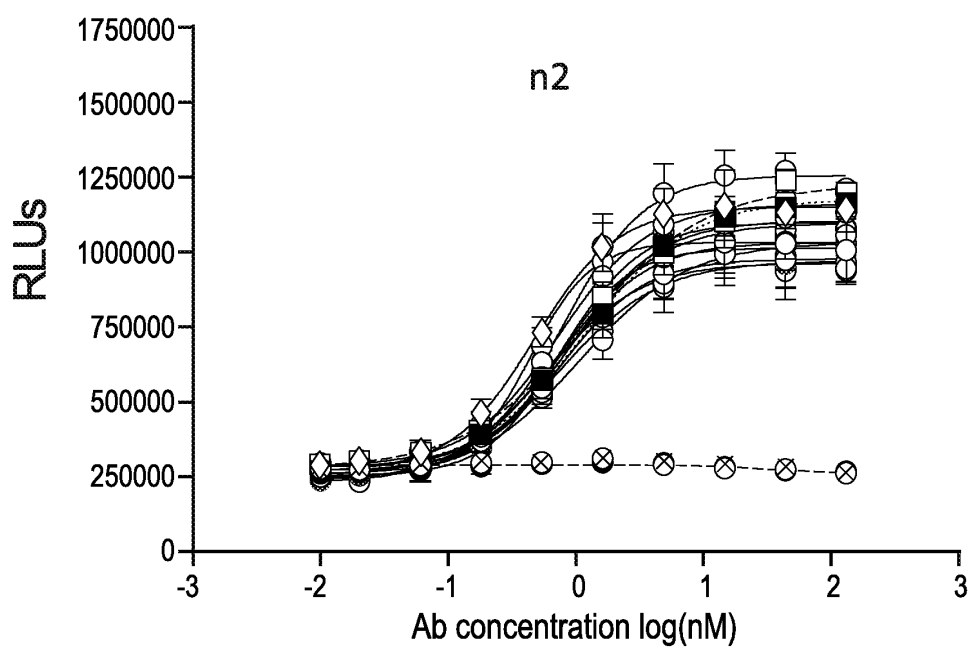
**Fig. 21A****Fig. 21B**

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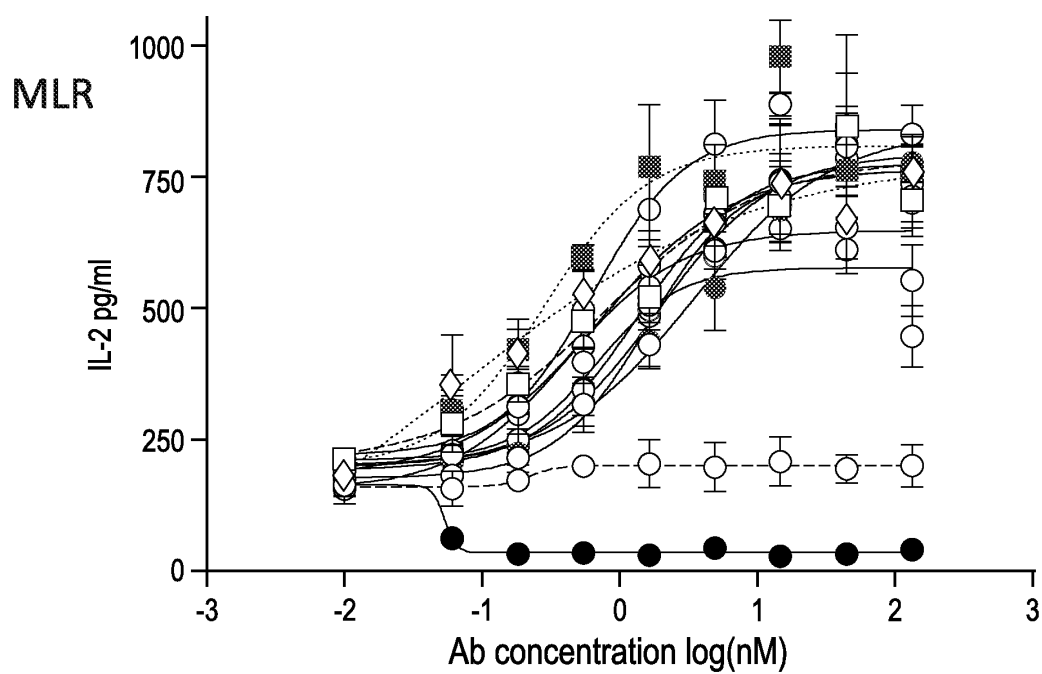
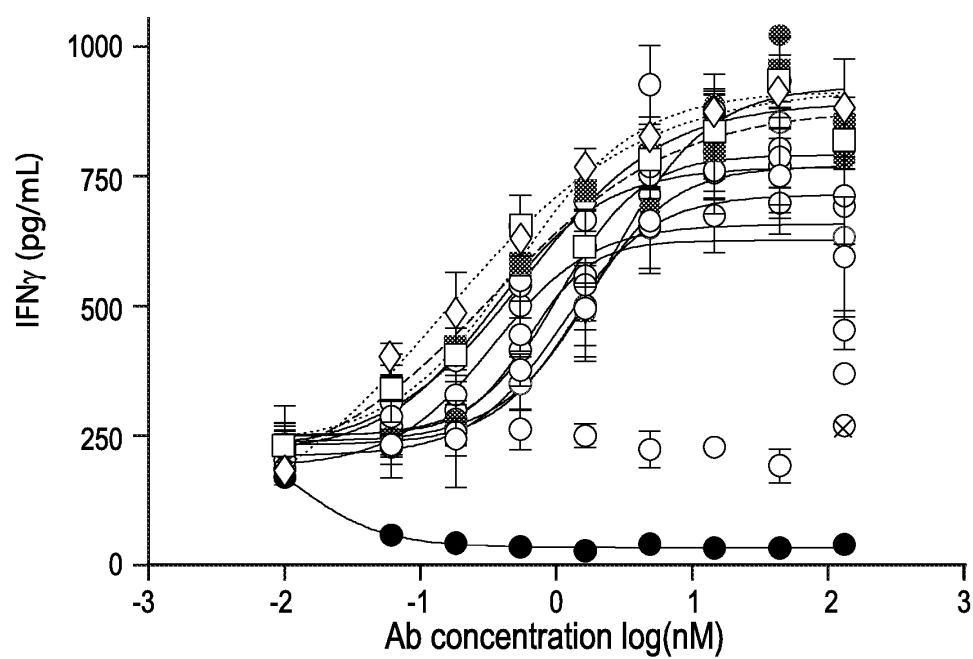
**Fig. 21C****Fig. 21D**



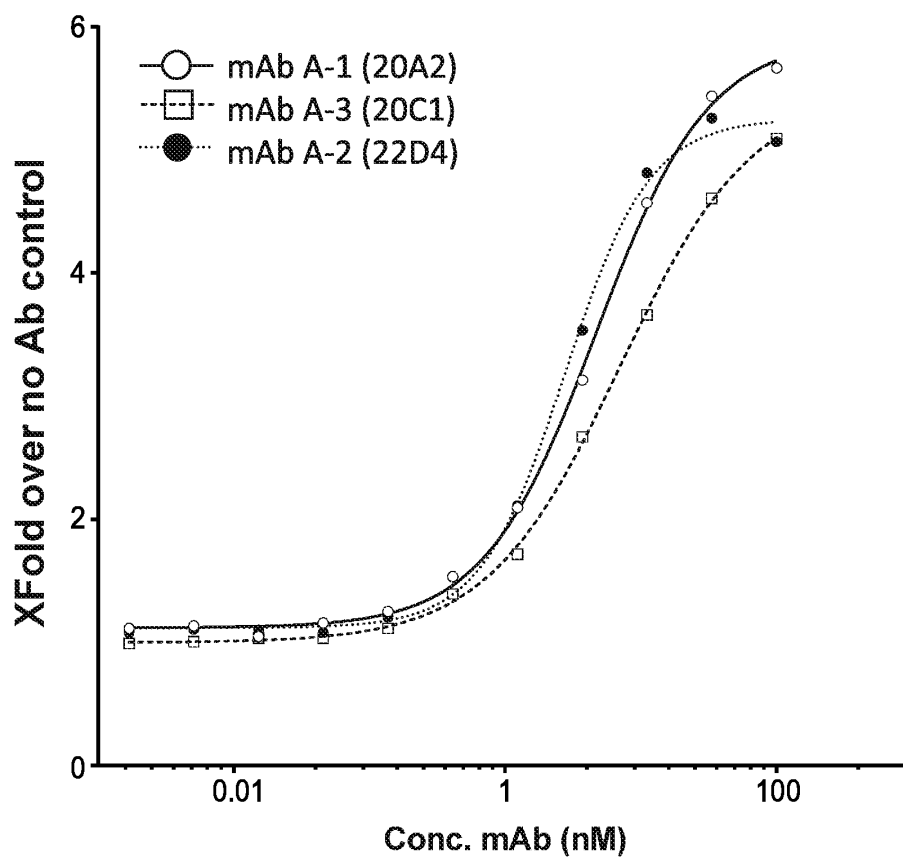
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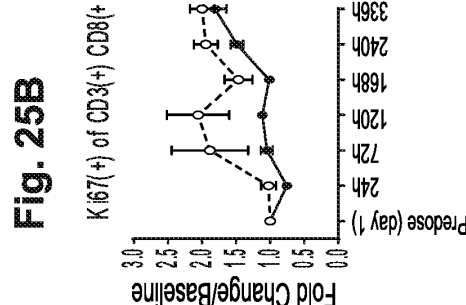
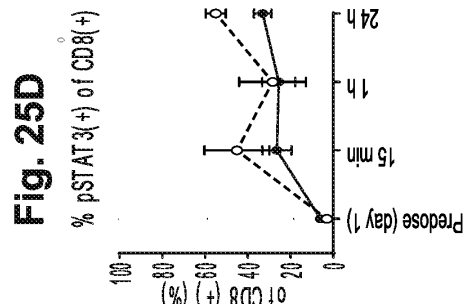
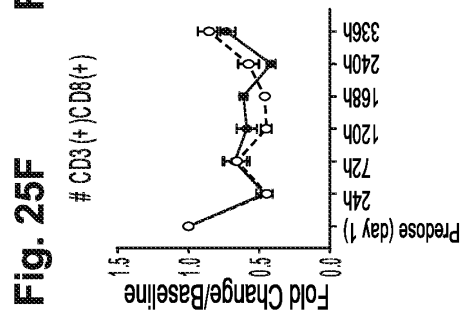
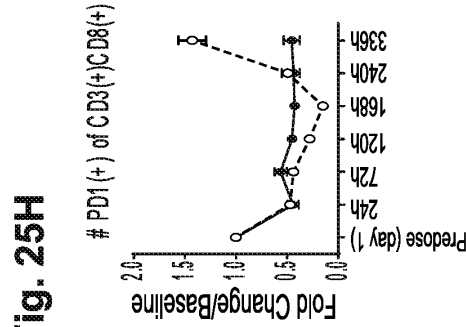
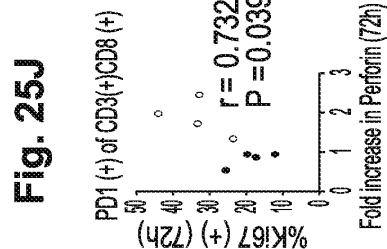
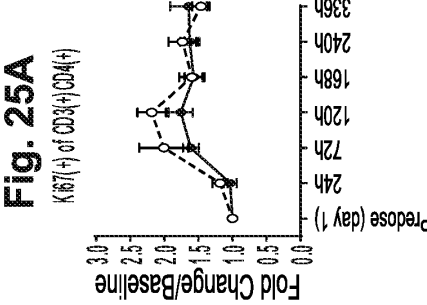
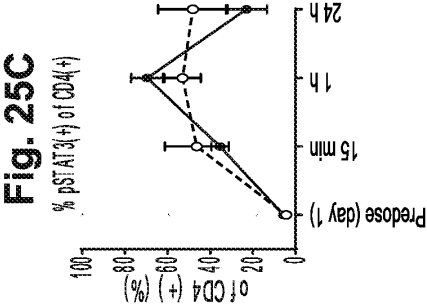
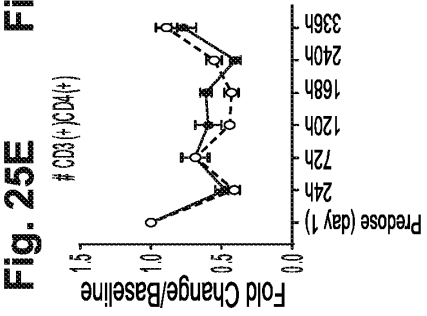
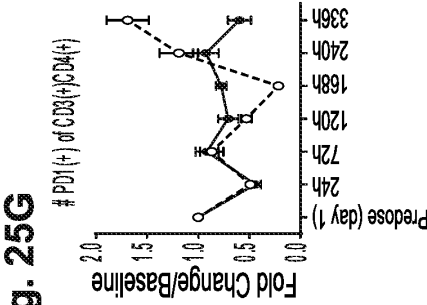
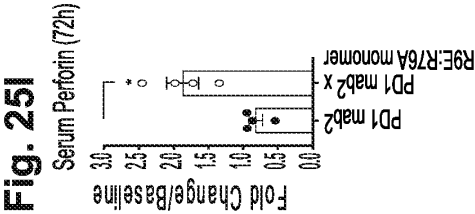
**Fig. 23A****Fig. 23B**

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Fig. 23C**Fig. 23D**

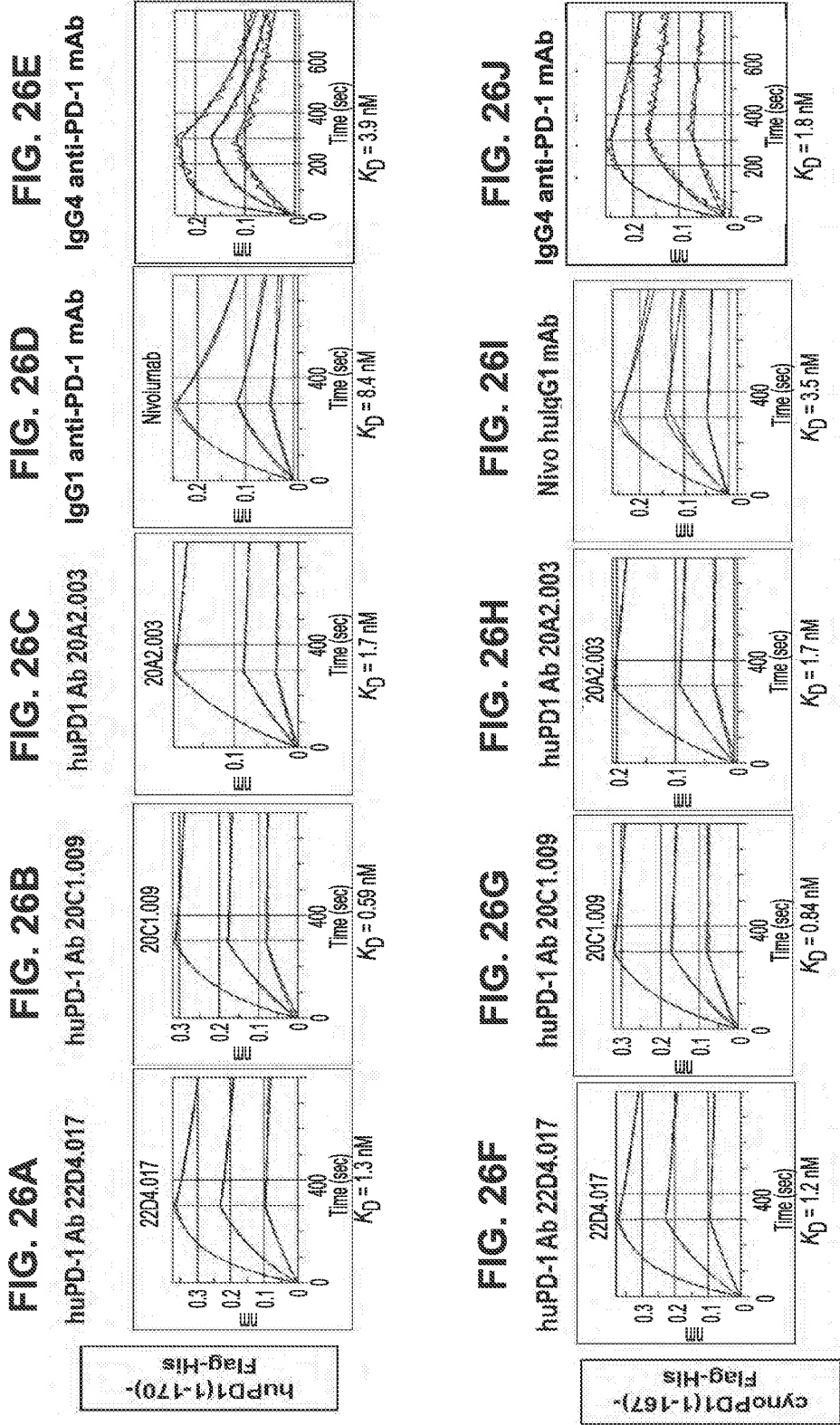
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**Fig. 24**

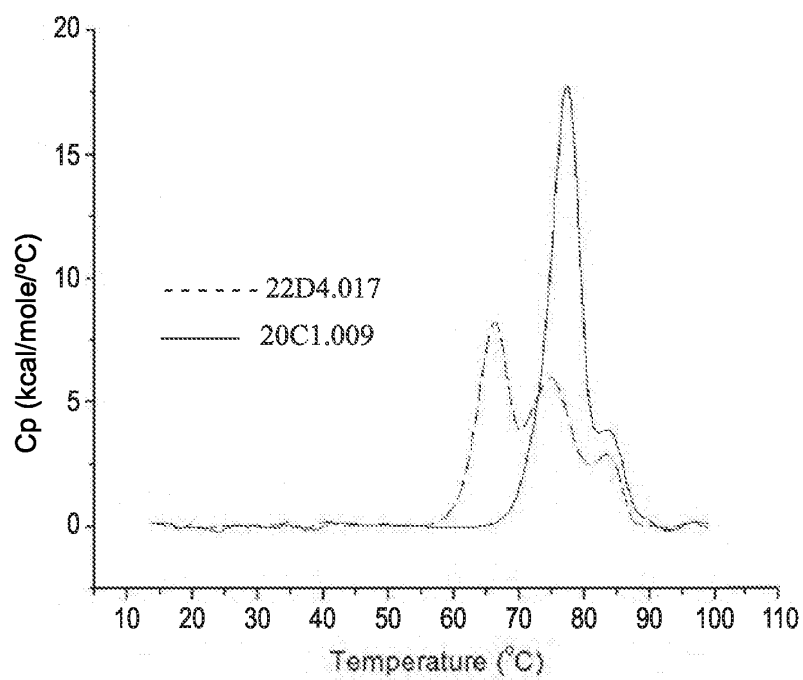


--○-- [22D4.017]-[R9E:R76A] (monomer)

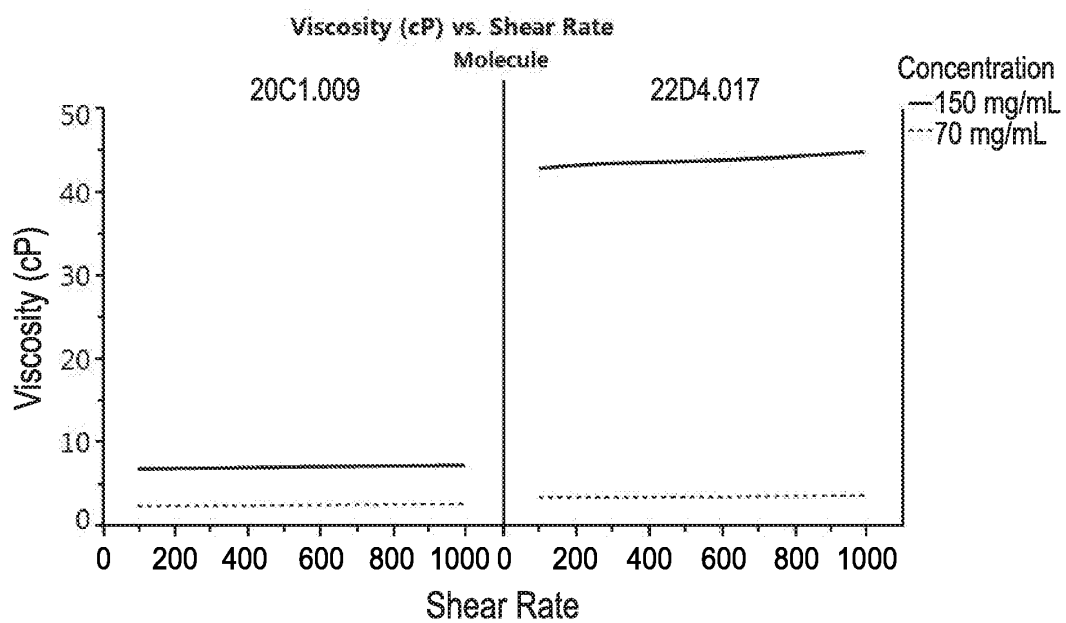
—●— [22D4.017]



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**Fig. 27**

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**Fig. 28**

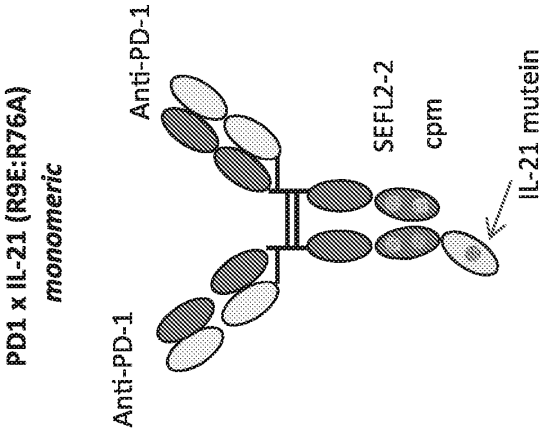
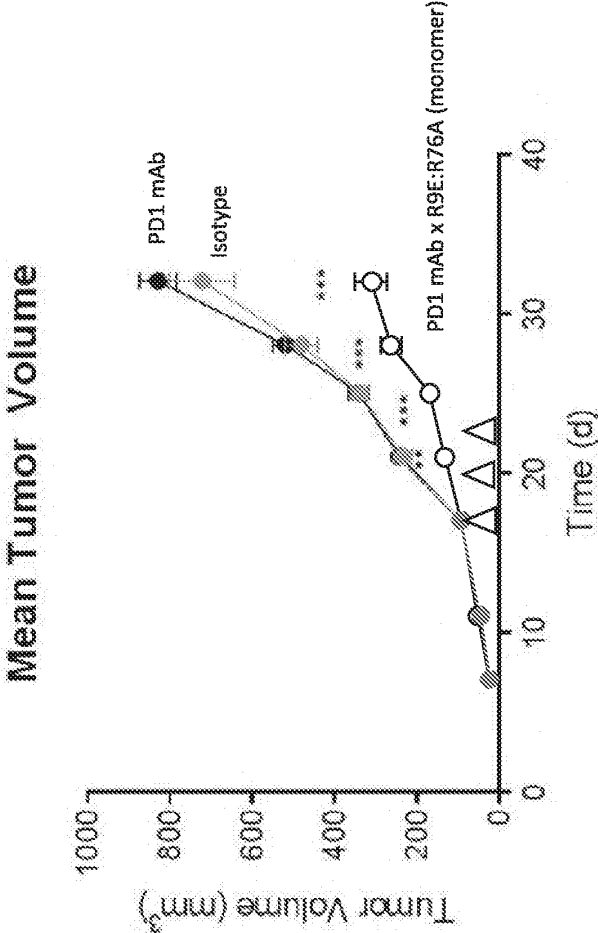
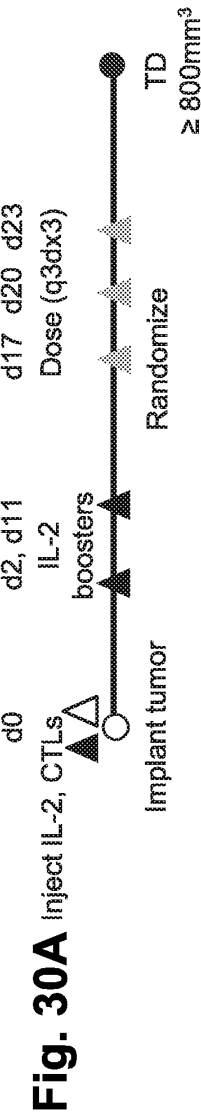


Fig. 30F

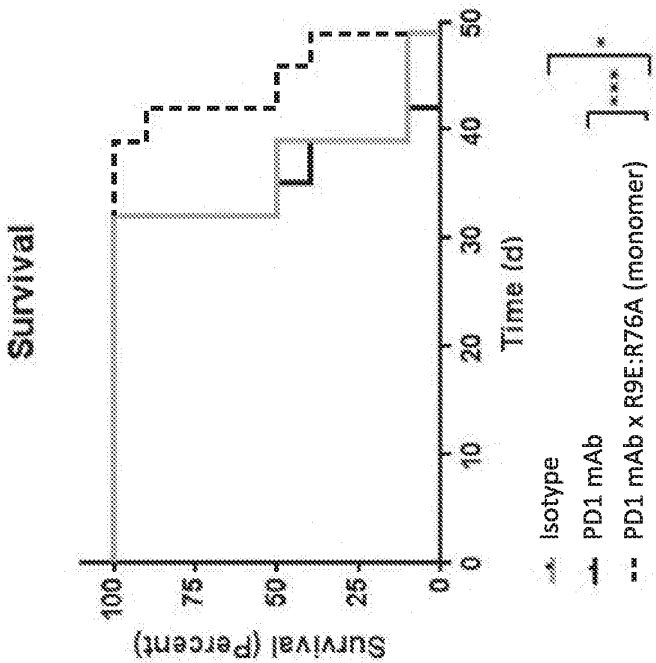


Fig. 30E

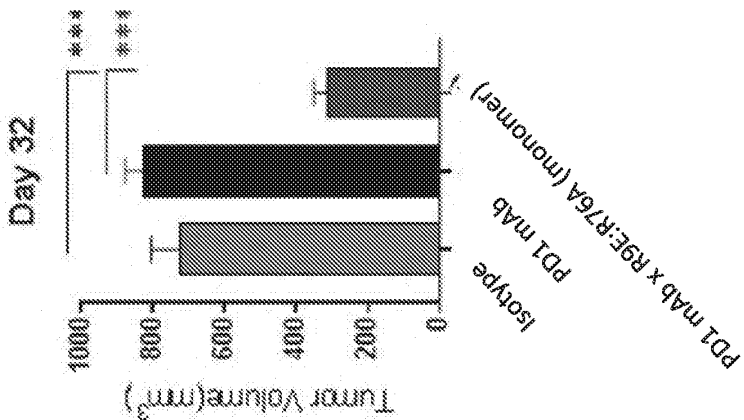
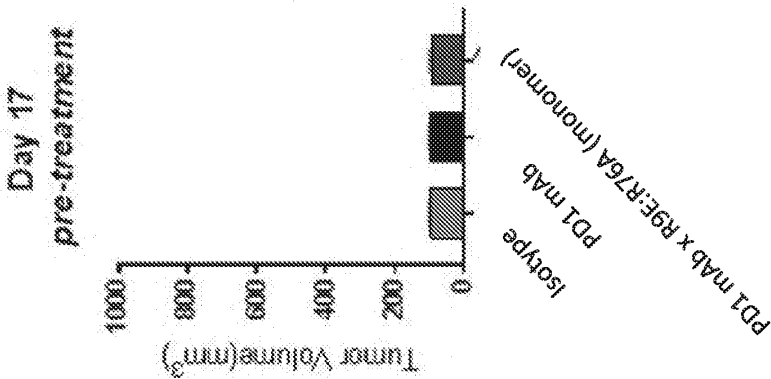


Fig. 30D



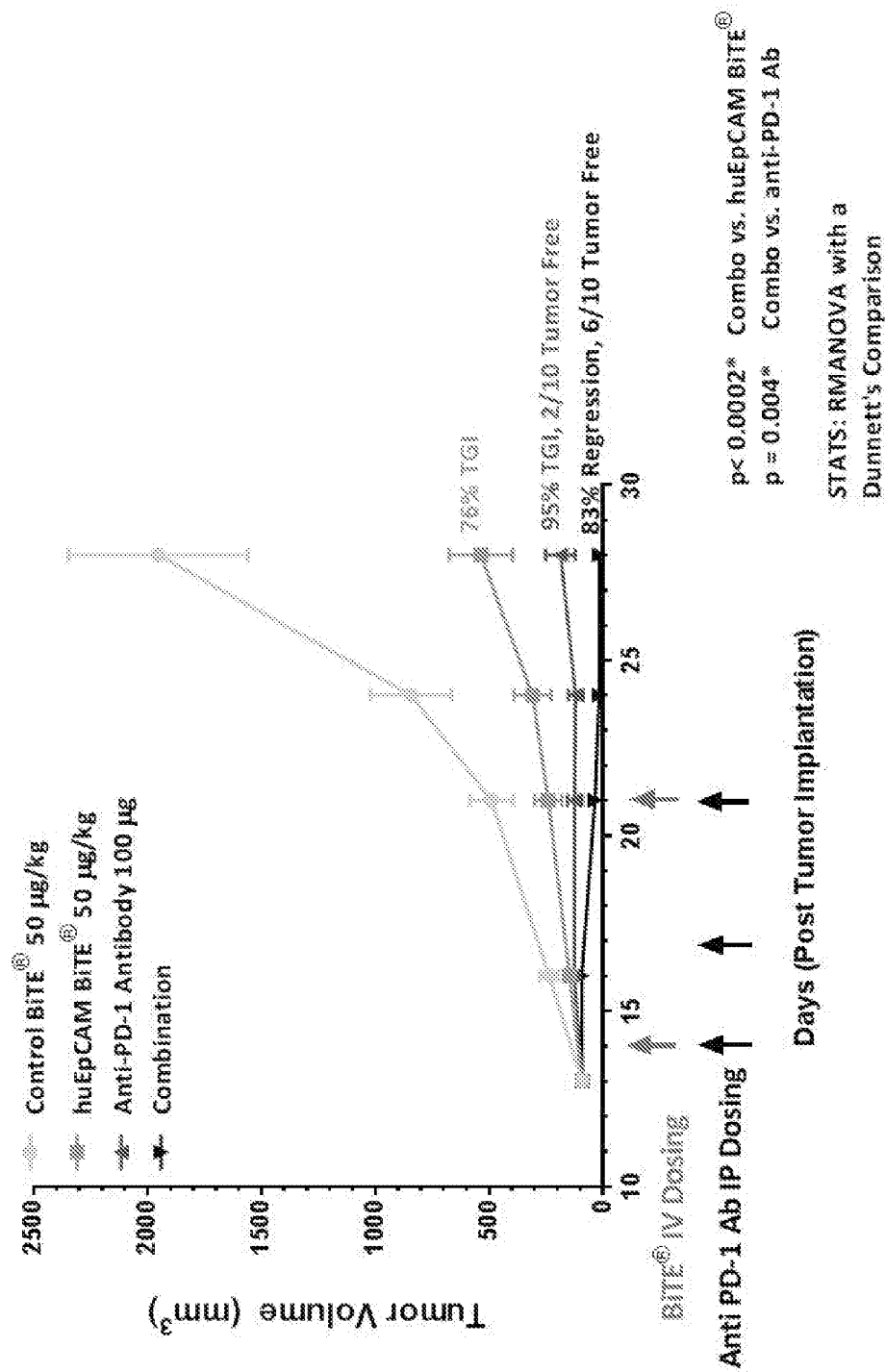
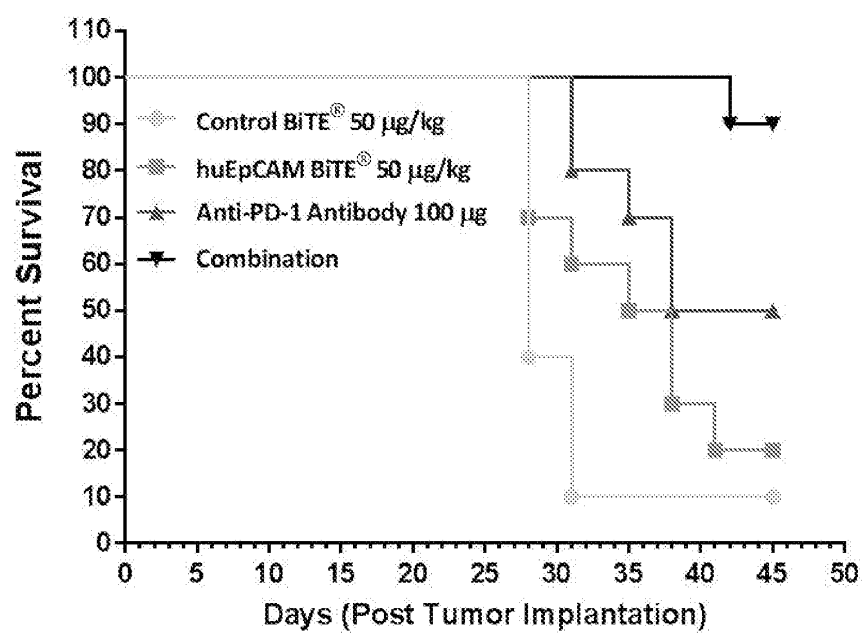
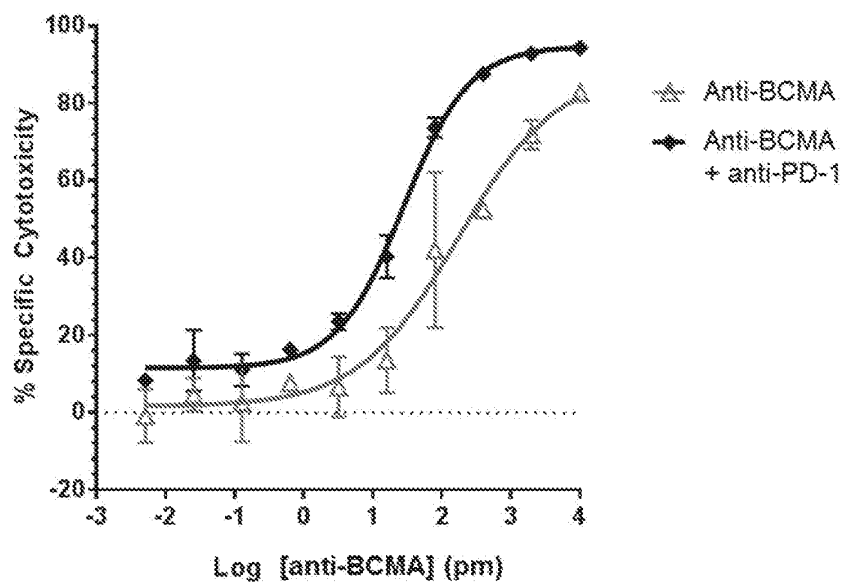
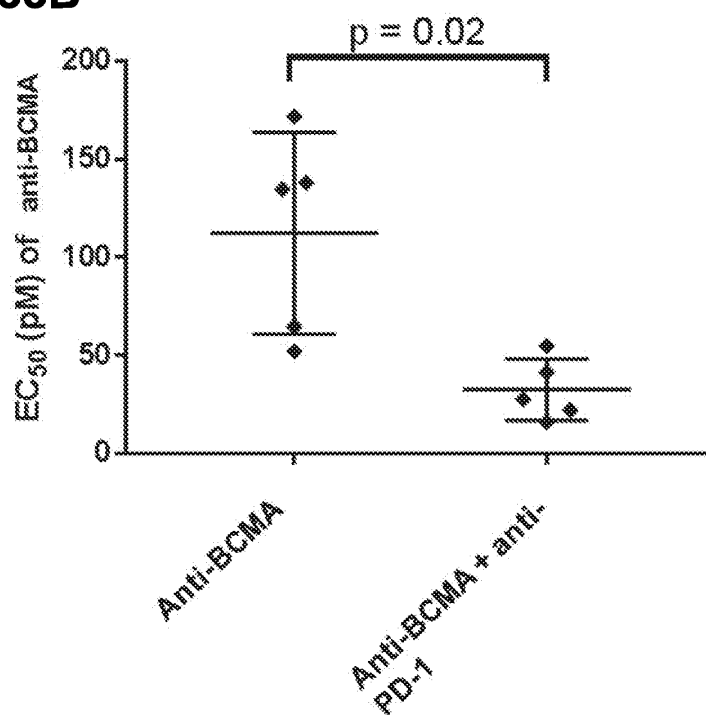


Fig. 31

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**Fig. 32**

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Fig. 33A**Fig. 33B**

SUBSTITUTE SHEET (RULE 26)

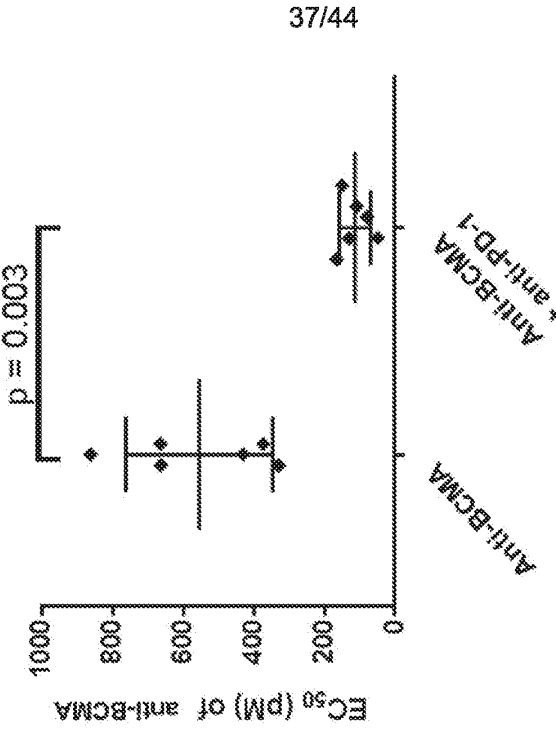


Fig. 34B

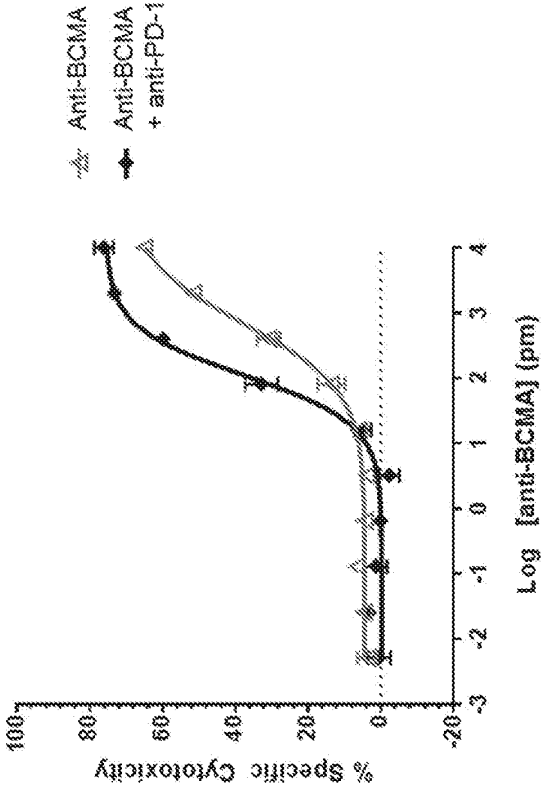
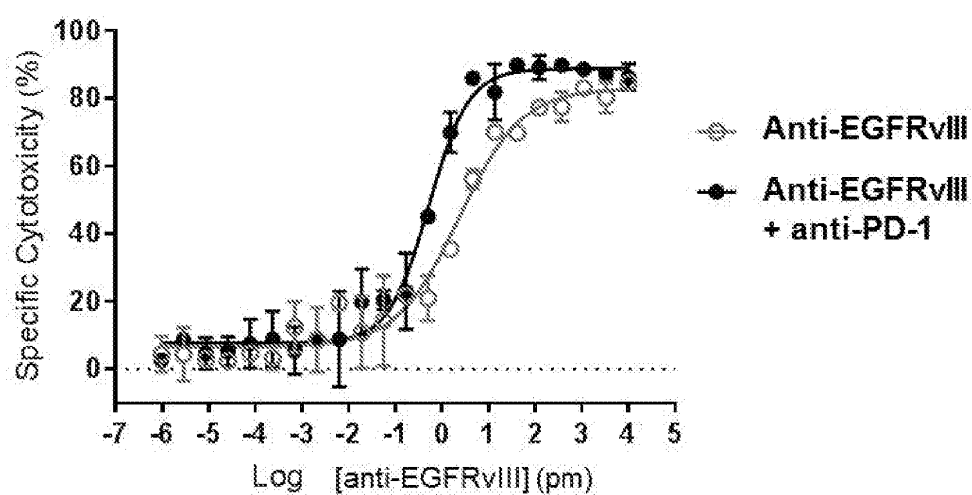
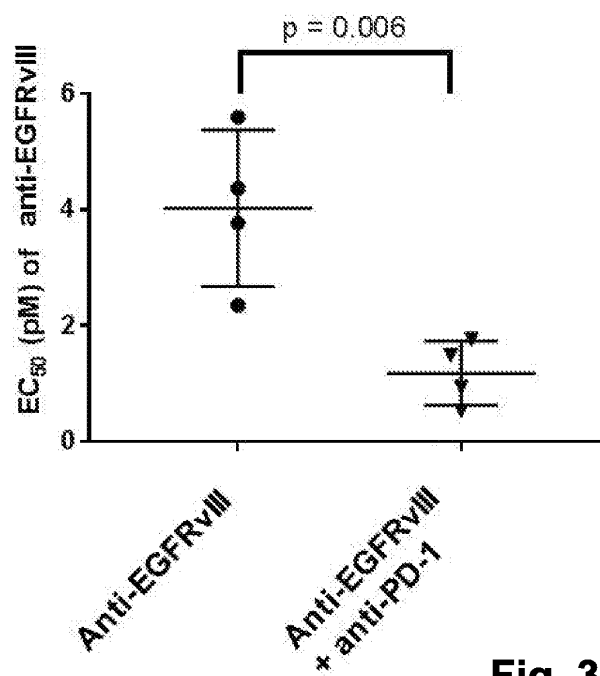


Fig. 34A

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**Fig. 35A****Fig. 35B**

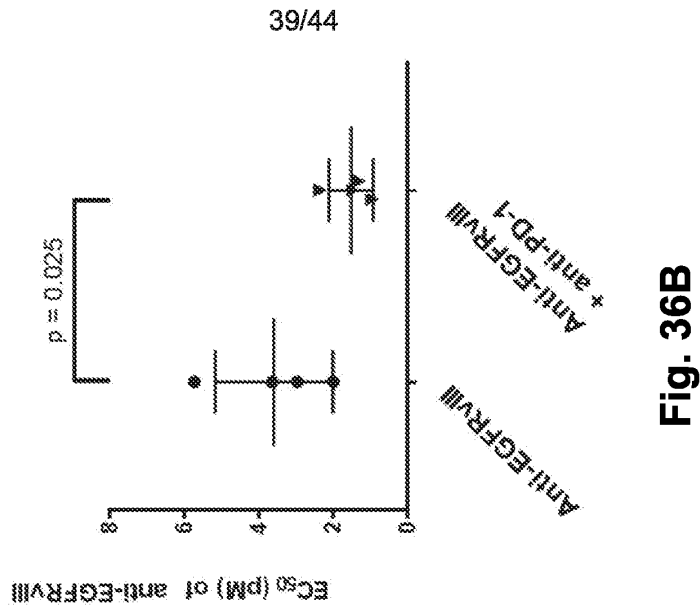


Fig. 36B

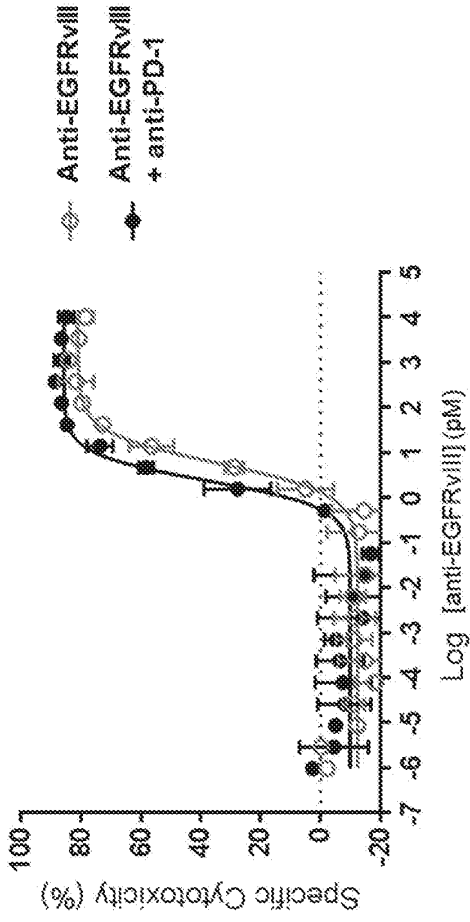
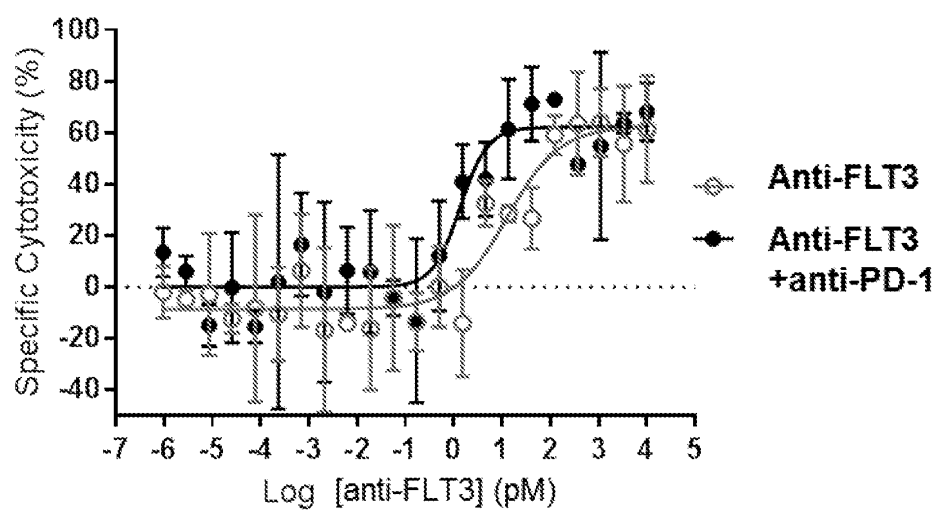
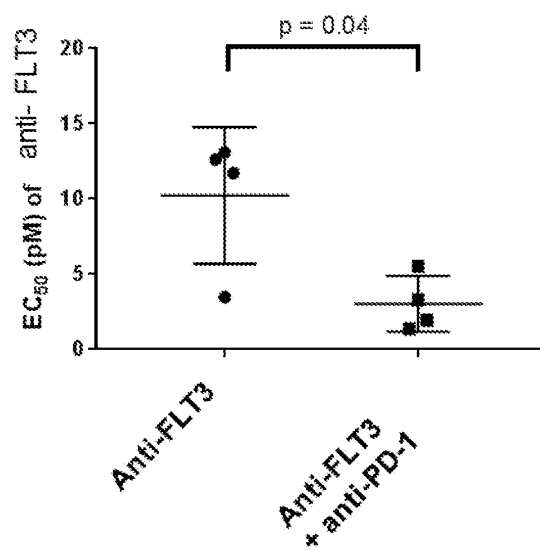
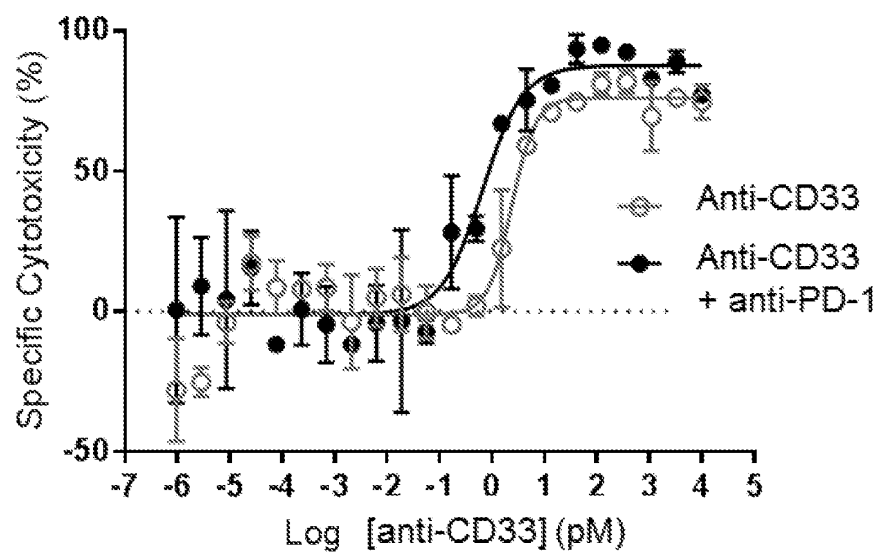
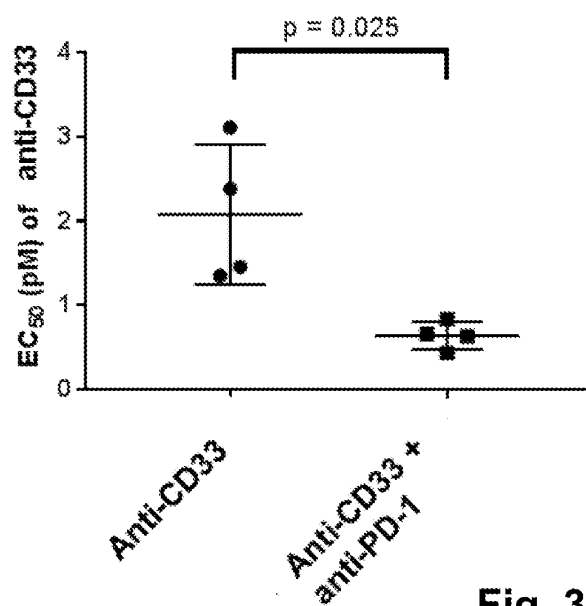


Fig. 36A

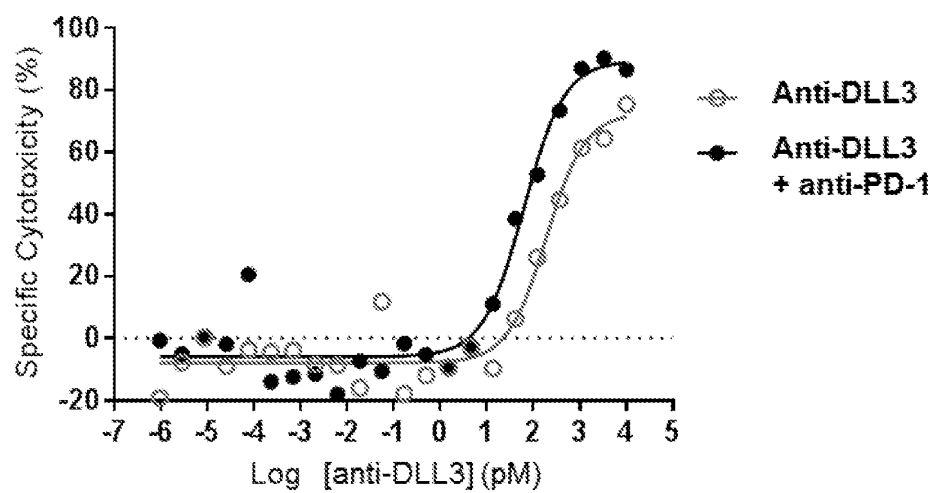
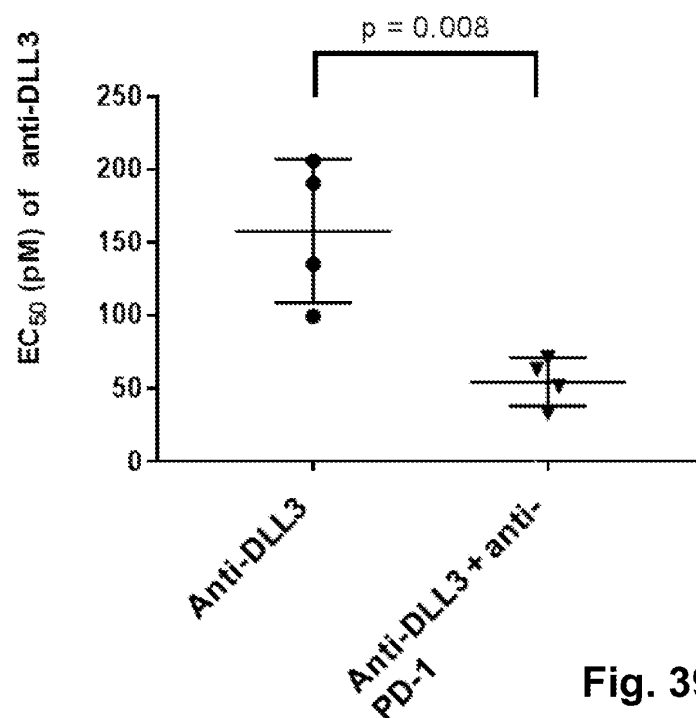
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**Fig. 37A****Fig. 37B**

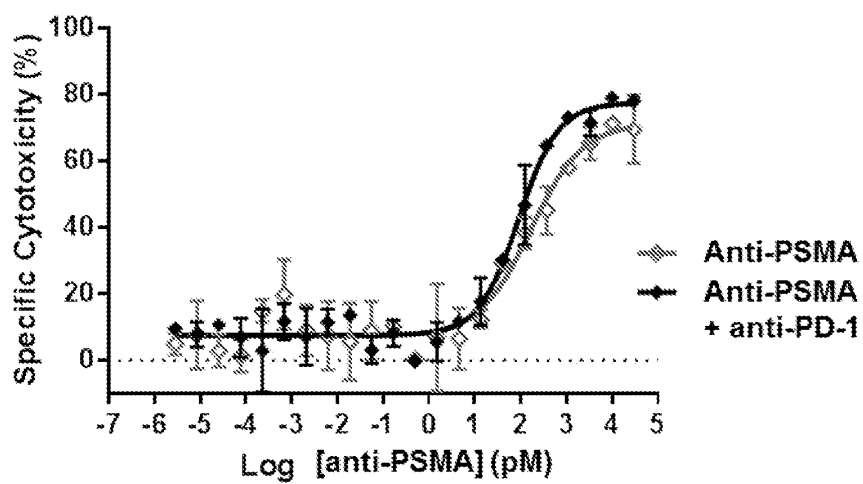
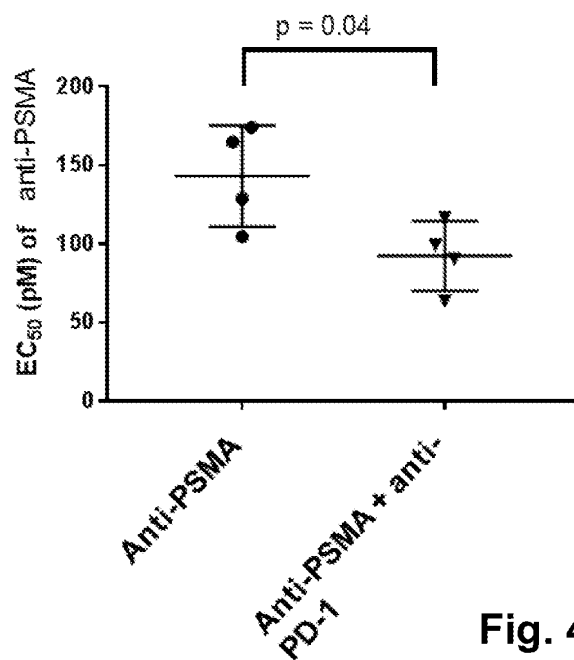
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**Fig. 38A****Fig. 38B**

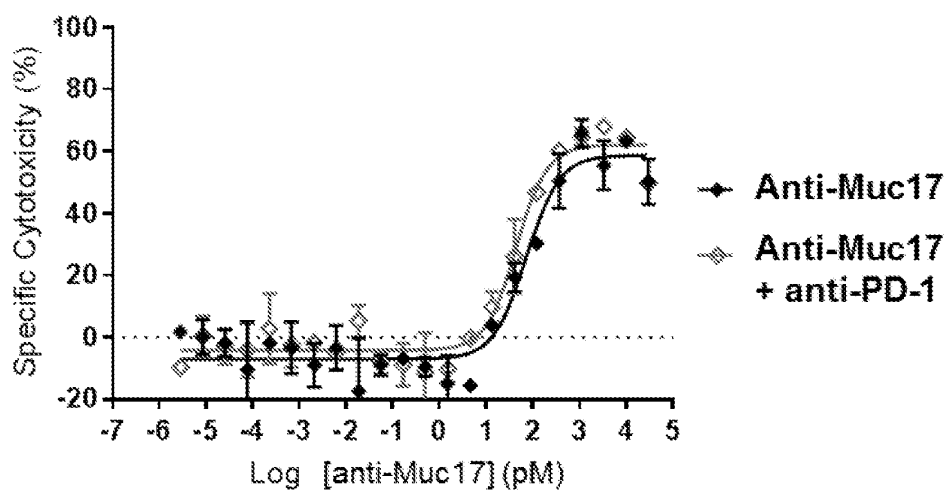
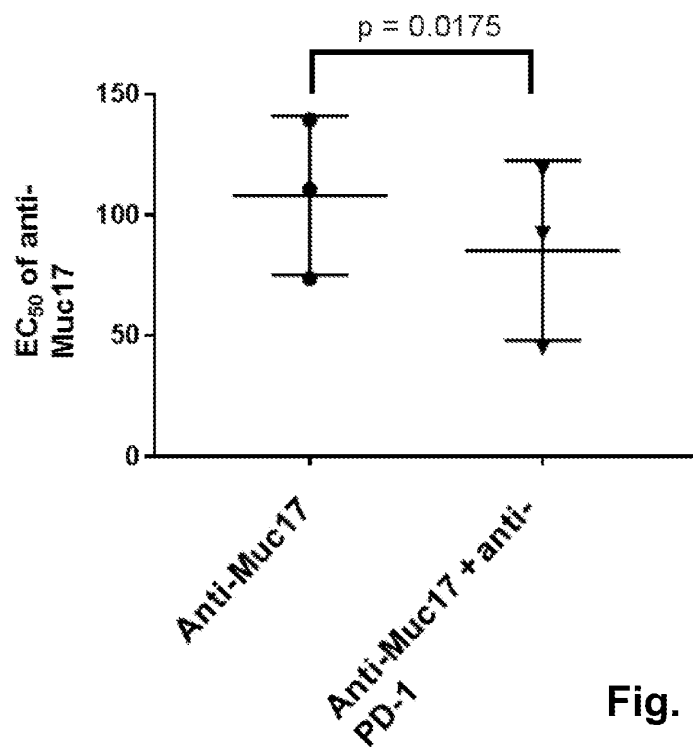
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**Fig. 39A****Fig. 39B**

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**Fig. 40A****Fig. 40B**

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**Fig. 41A****Fig. 41B**