

1/80

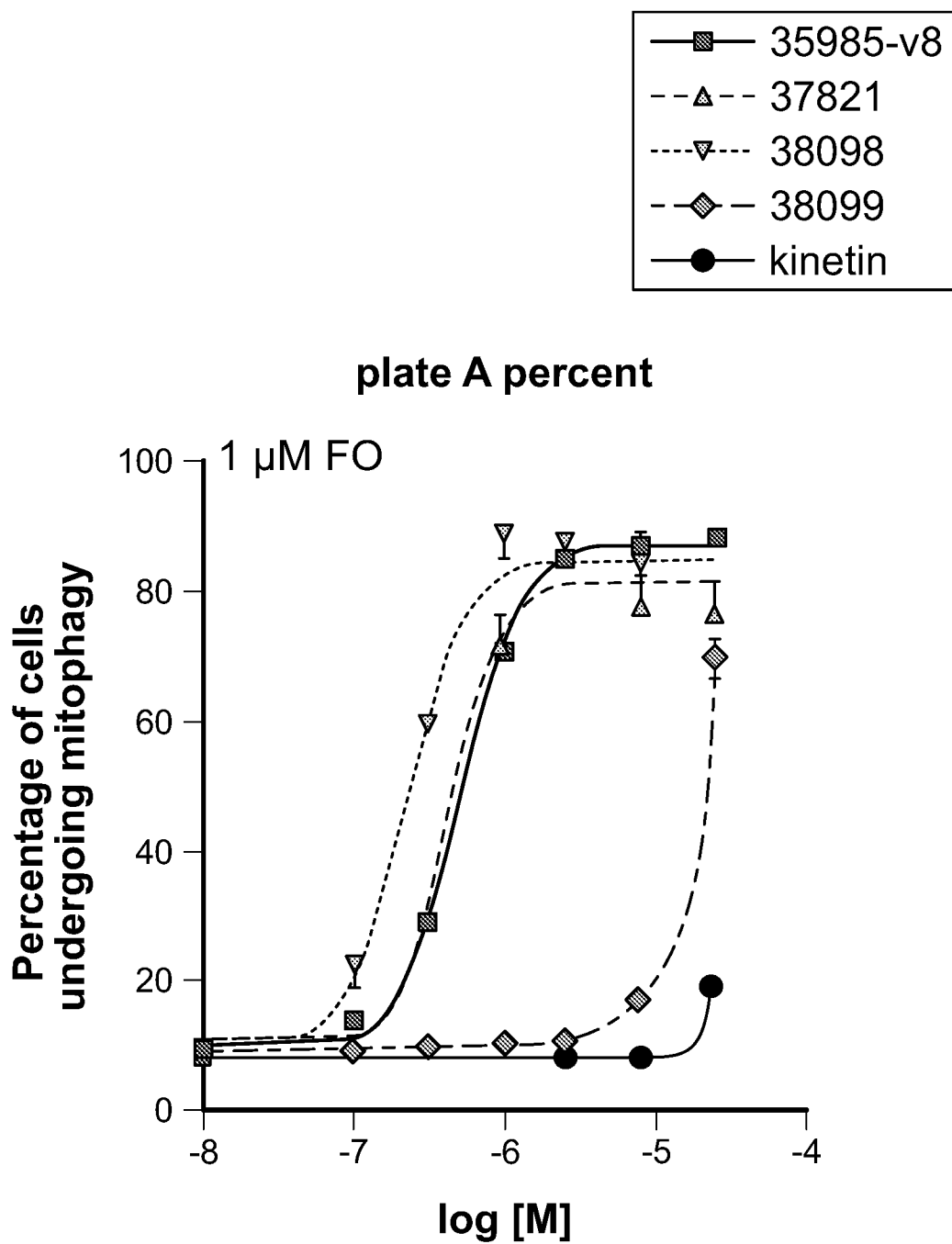


FIG. 1A

2/80

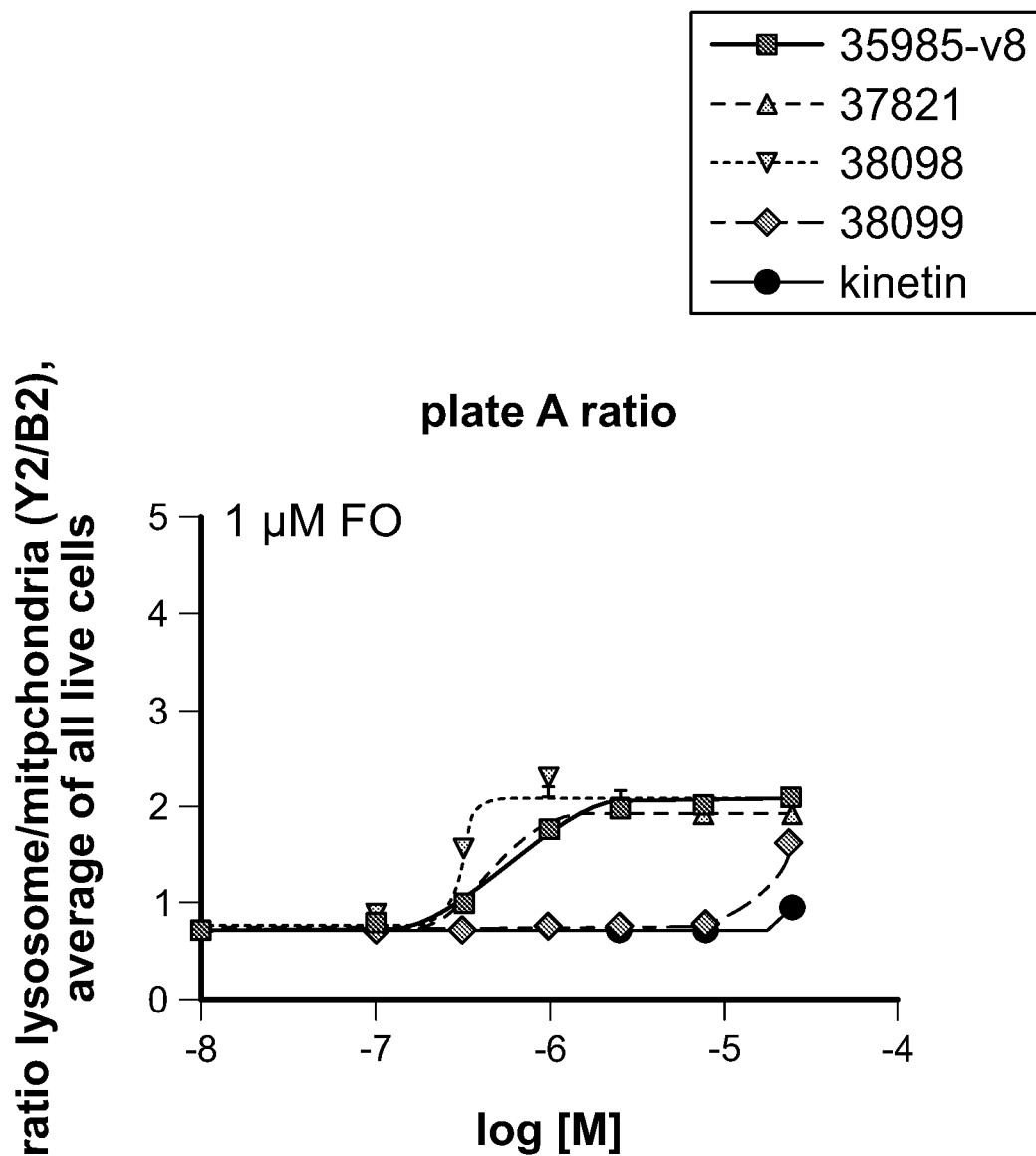


FIG. 1B

3/80

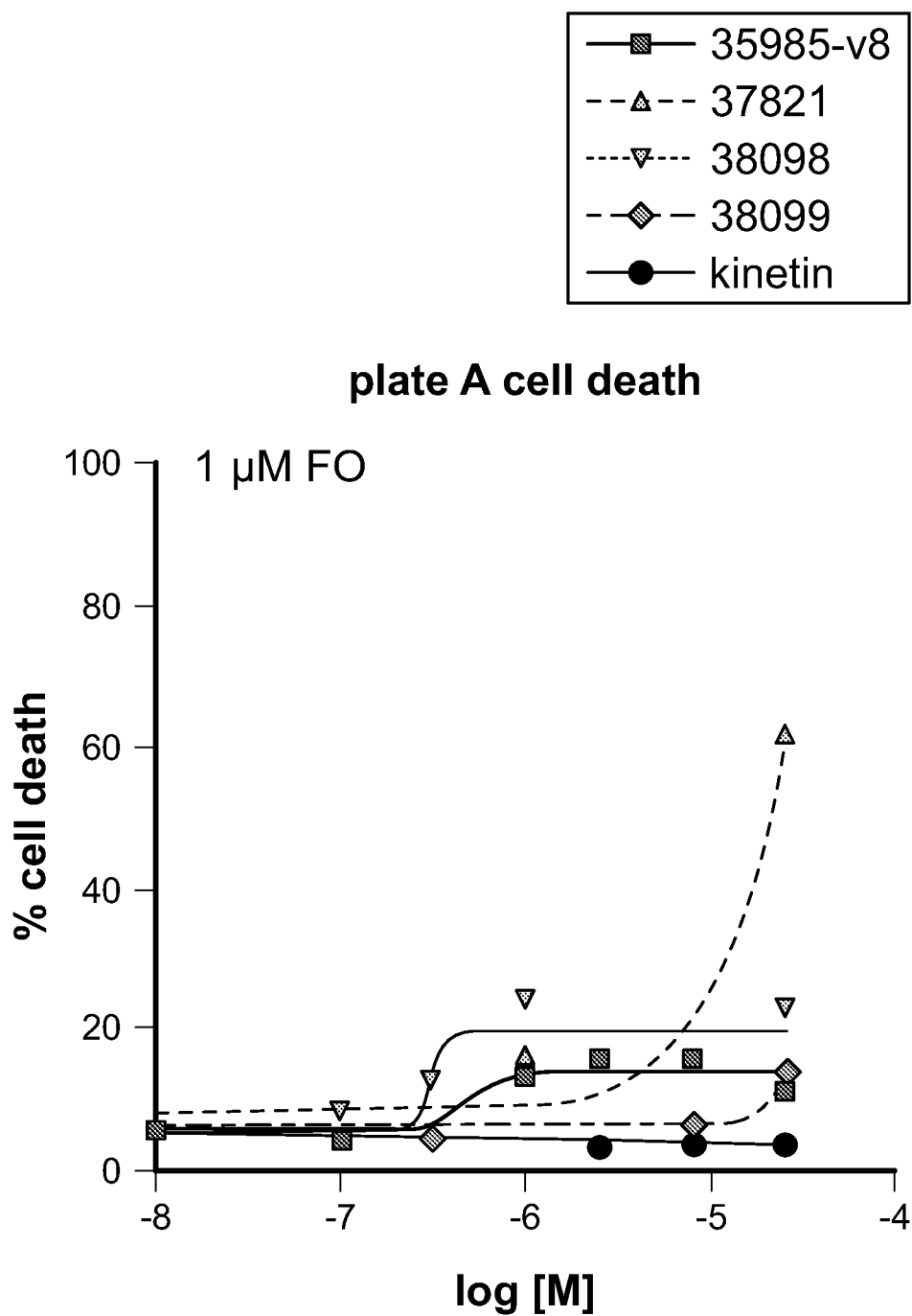


FIG. 1C

4/80

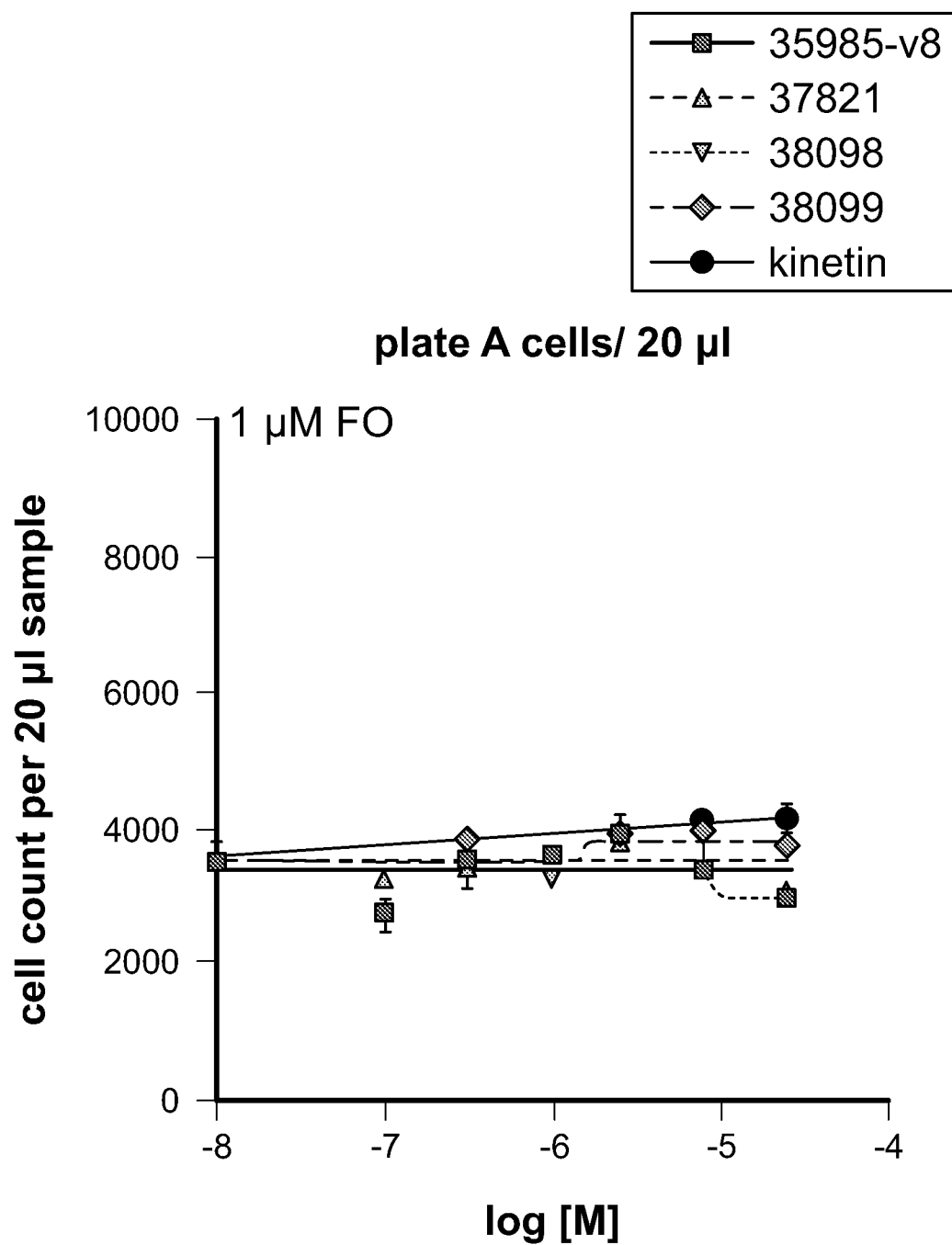


FIG. 1D

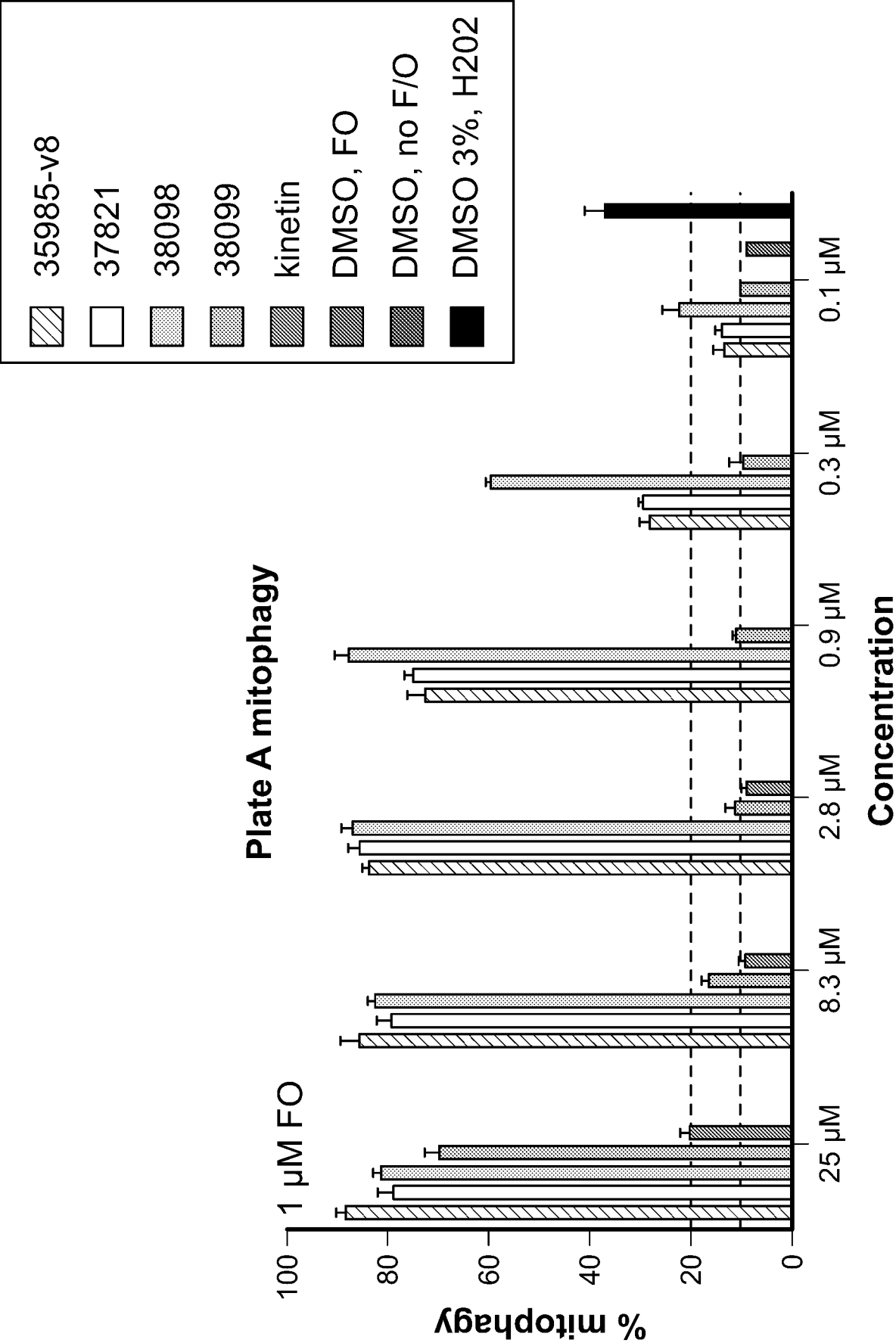


FIG. 1E

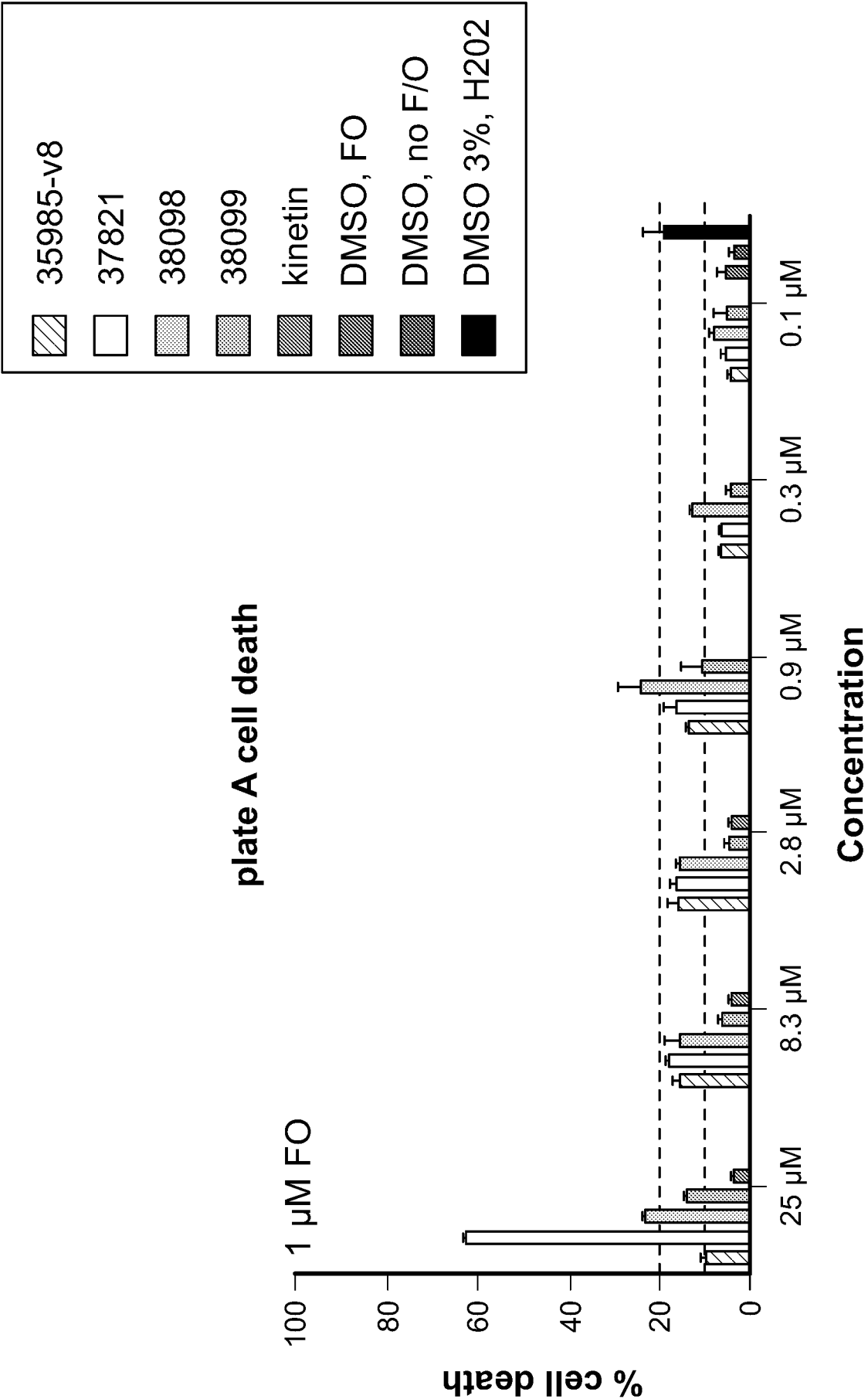


FIG. 1F

7/80

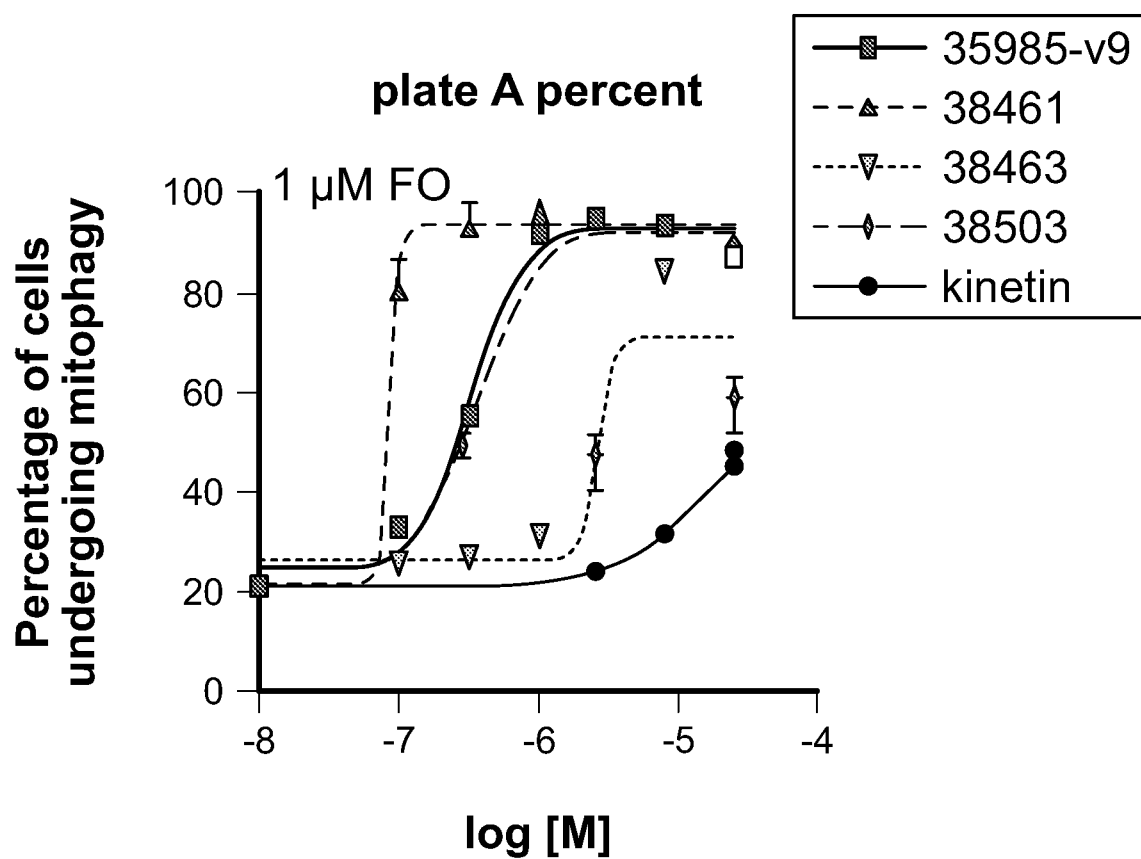


FIG. 2A

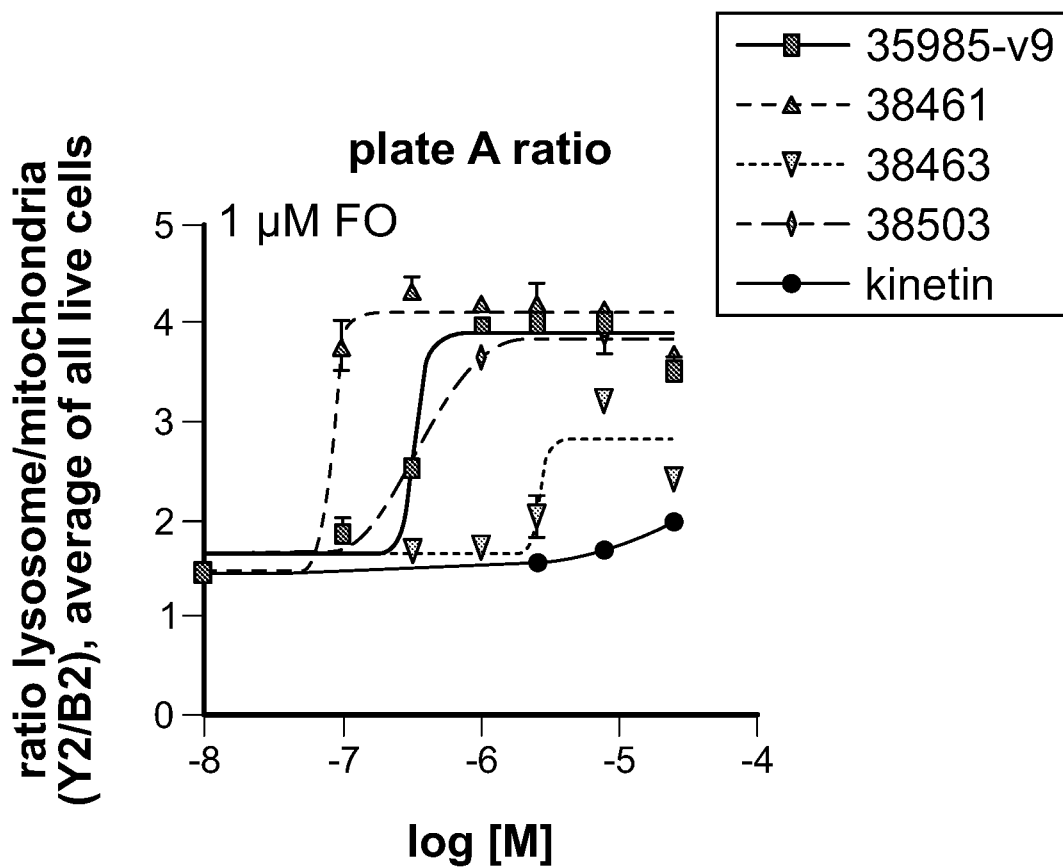


FIG. 2B

8/80

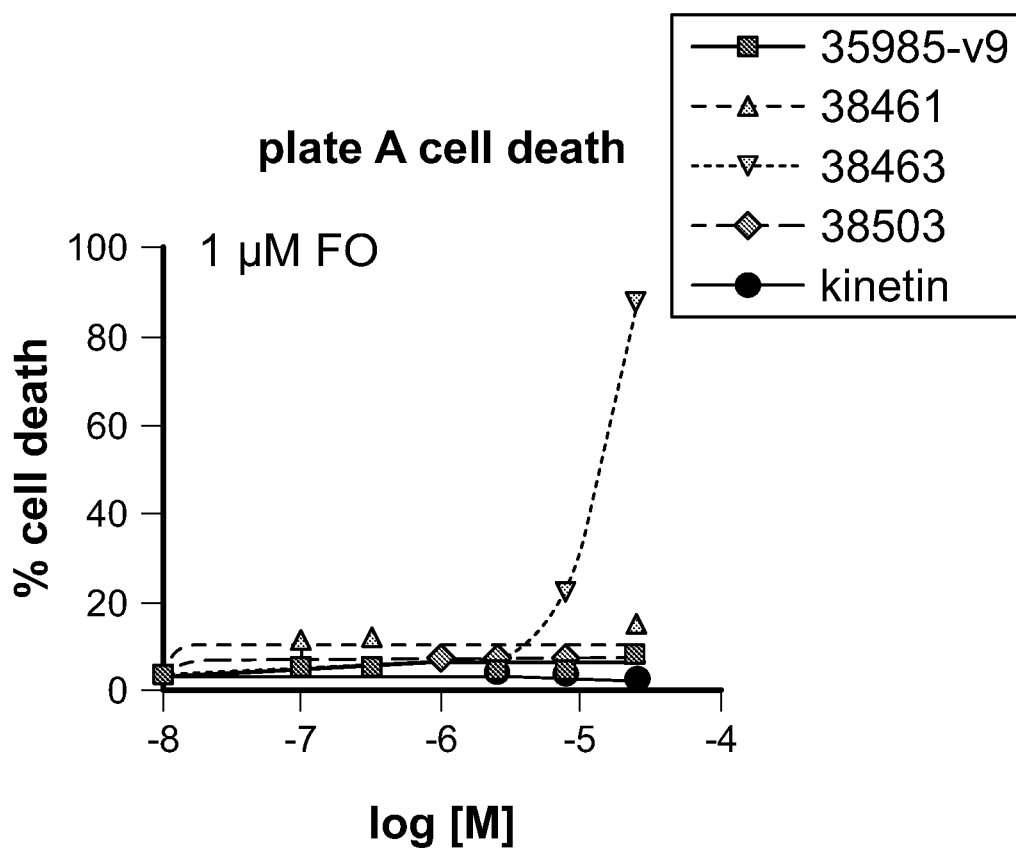


FIG. 2C

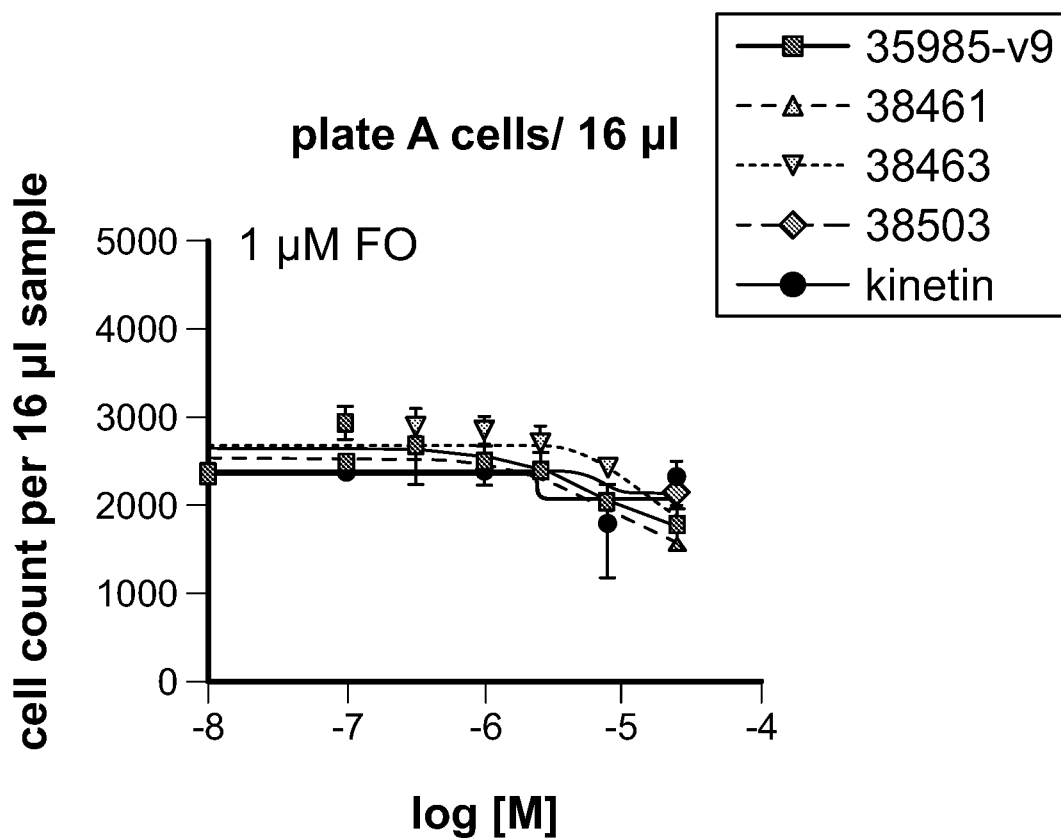


FIG. 2D

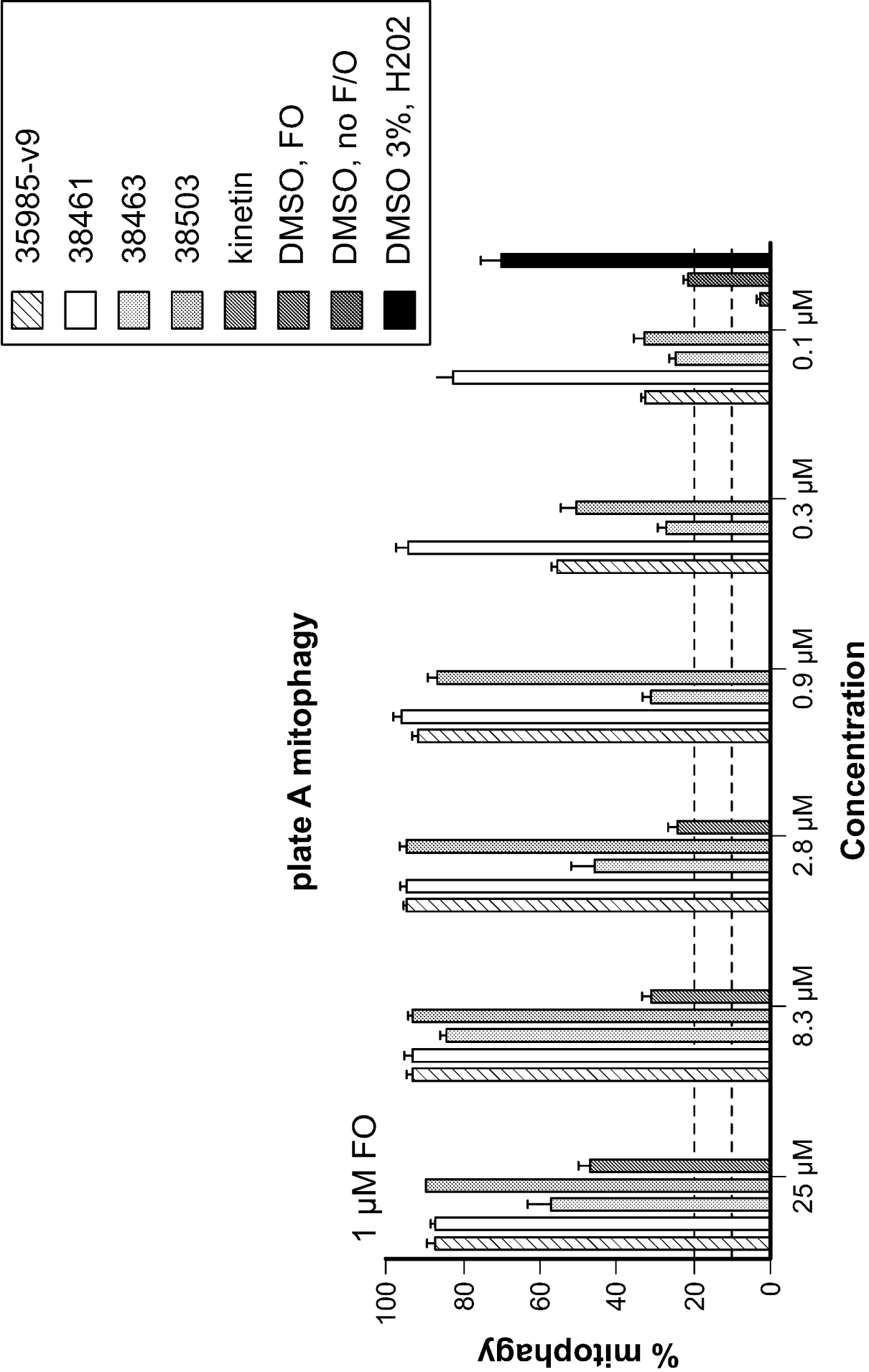


FIG. 2E

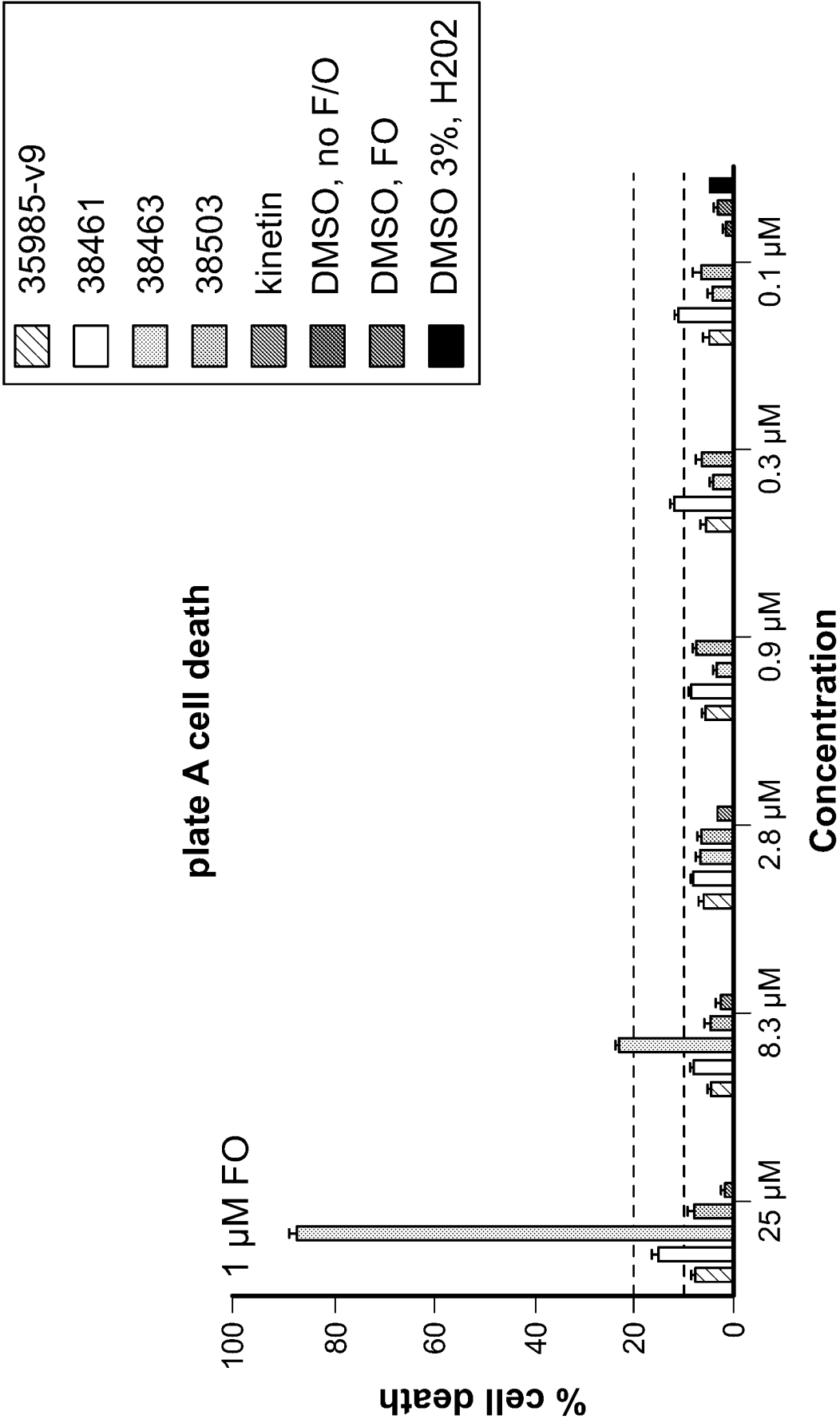


FIG. 2F

11/80

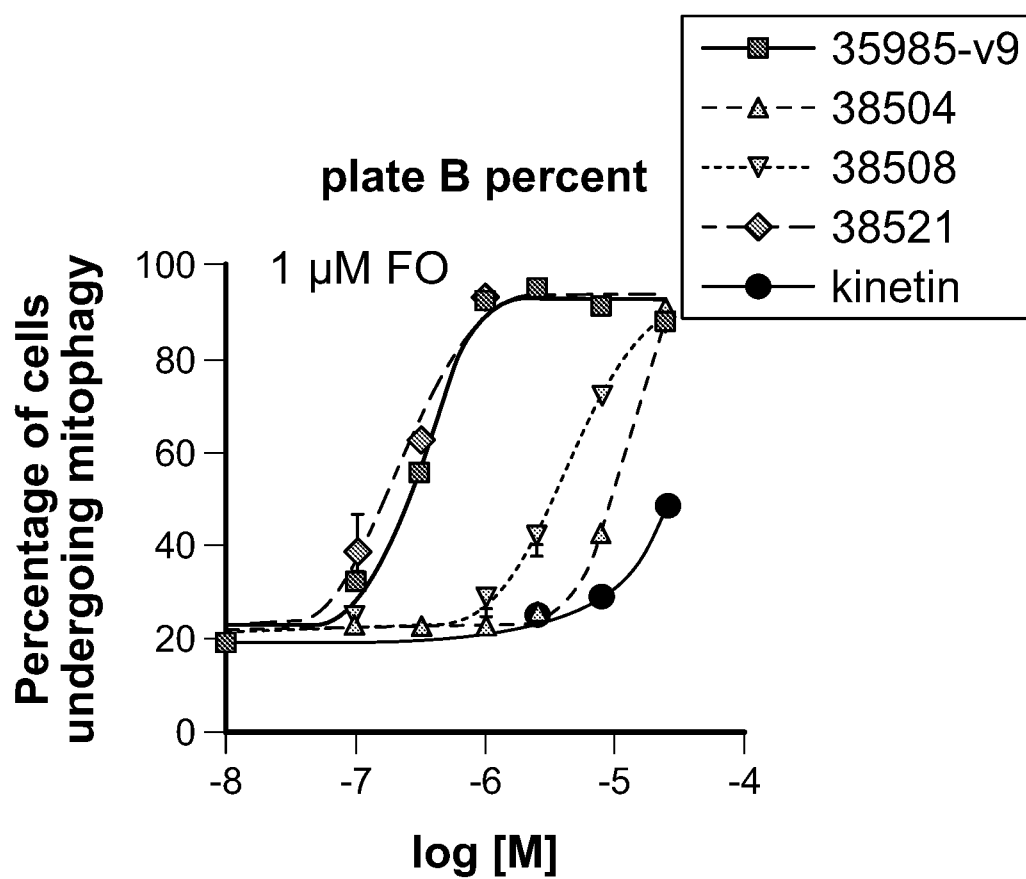


FIG. 3A

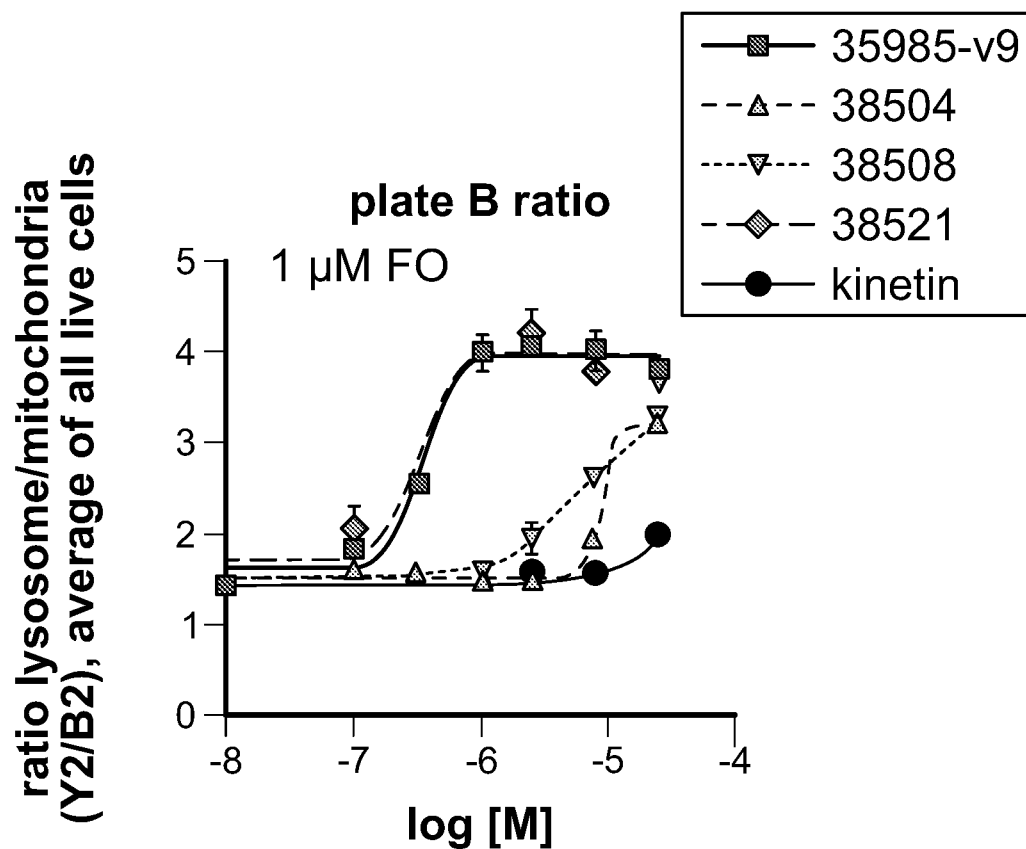


FIG. 3B

12/80

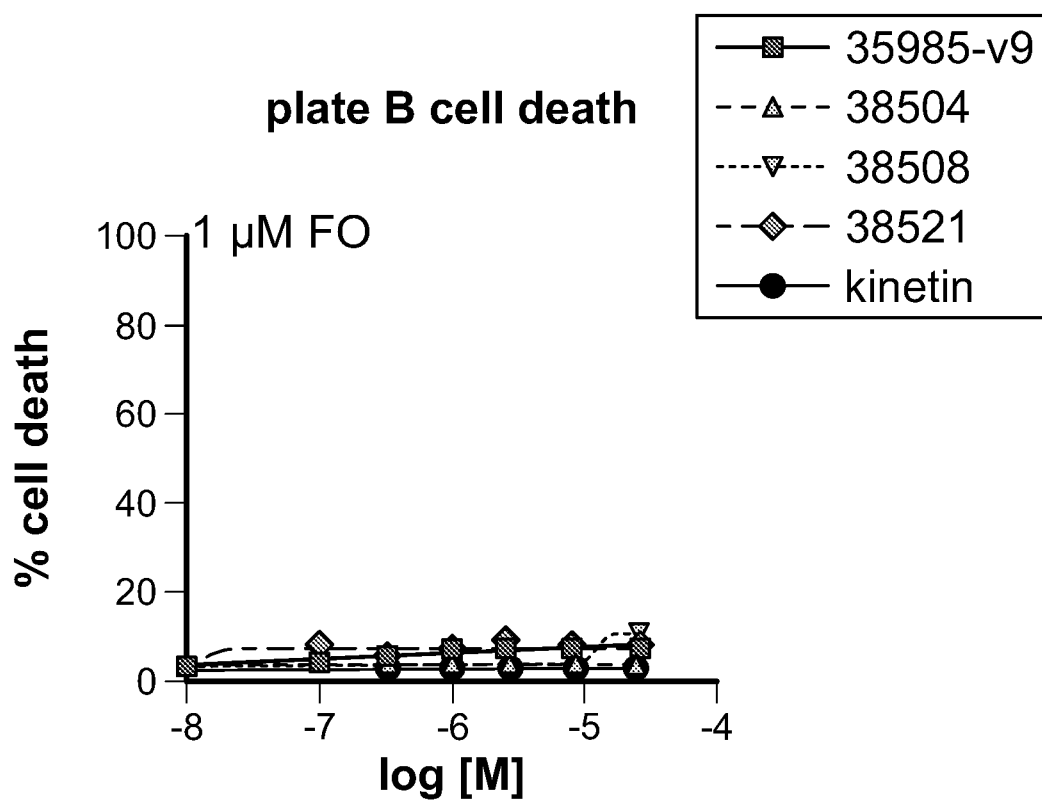


FIG.3C

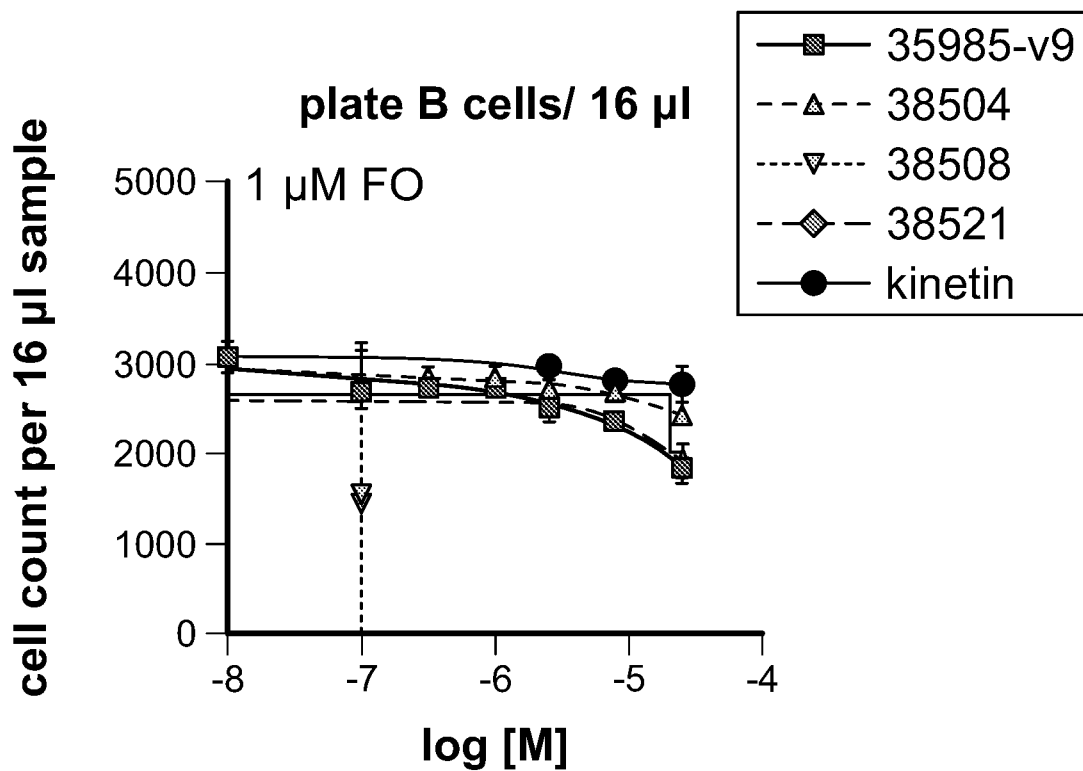


FIG. 3D

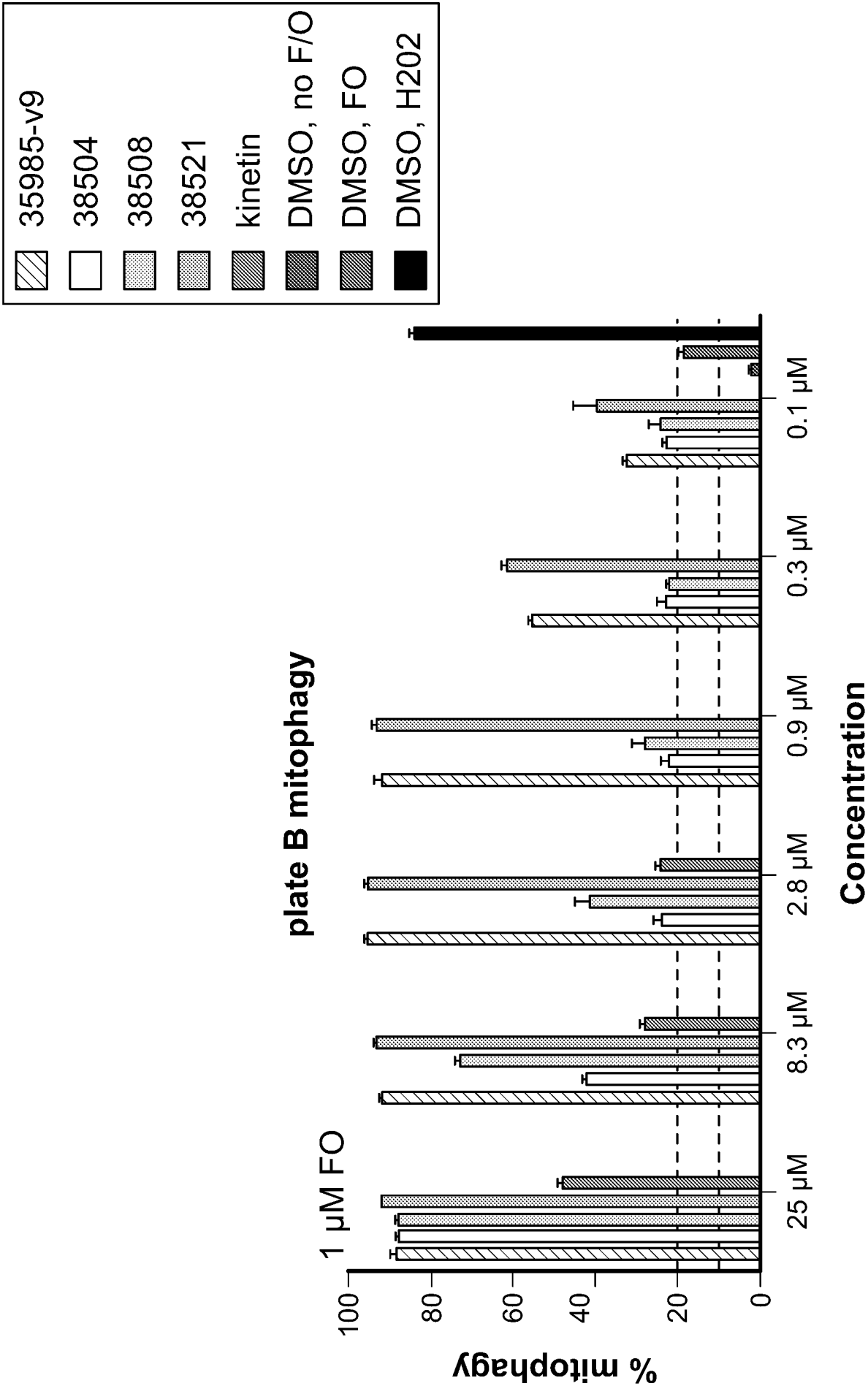


FIG. 3E

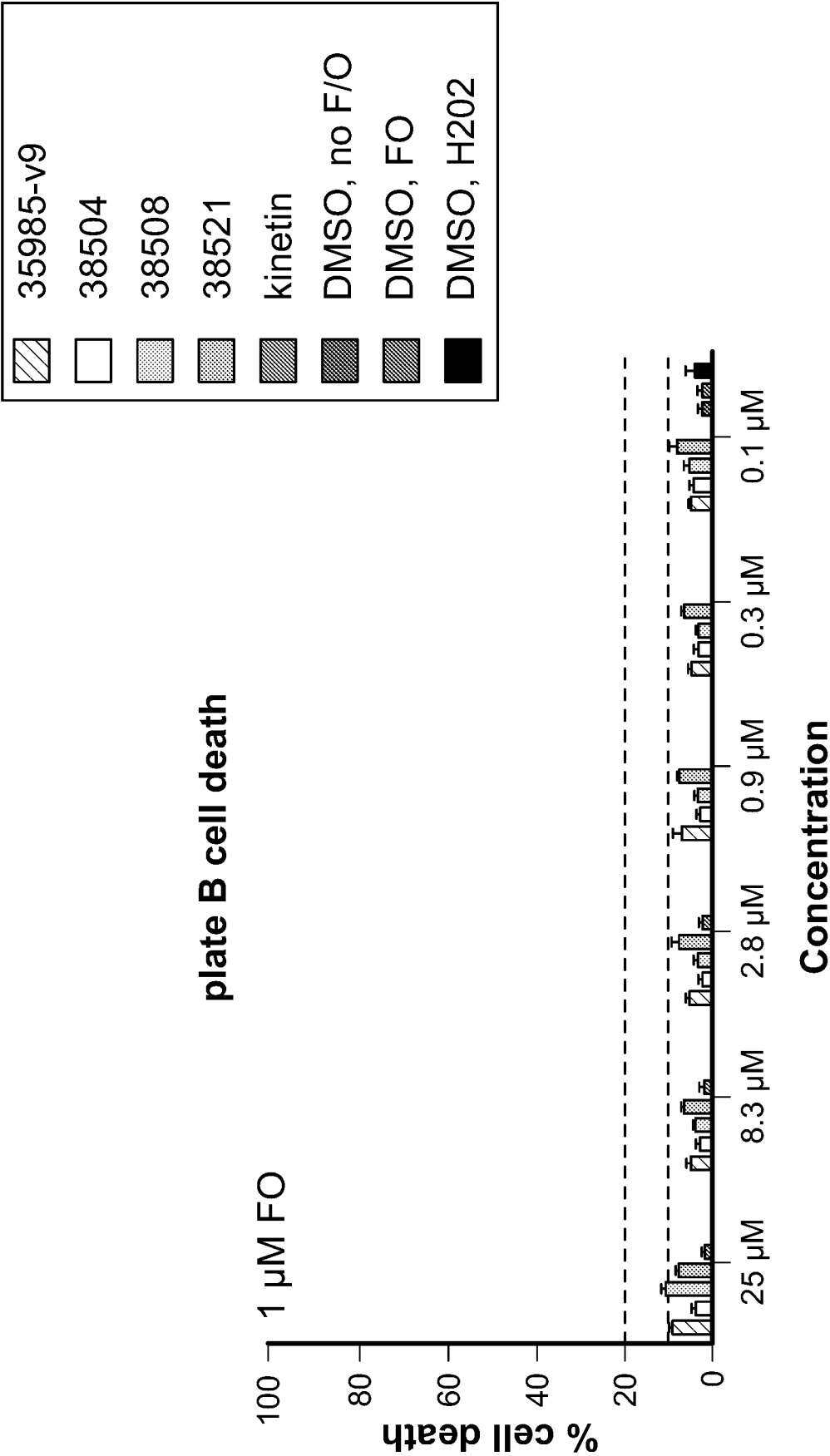


FIG. 3F

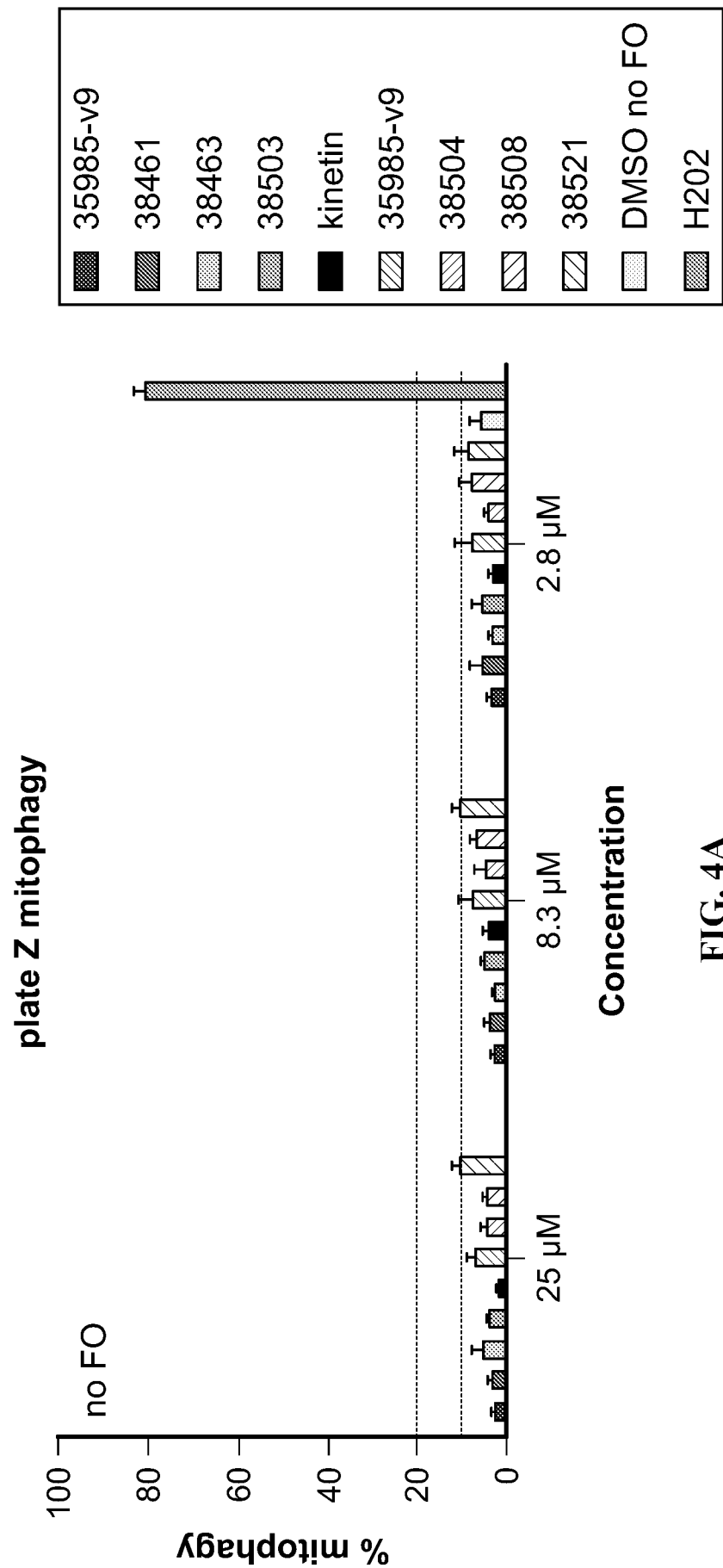


FIG. 4A

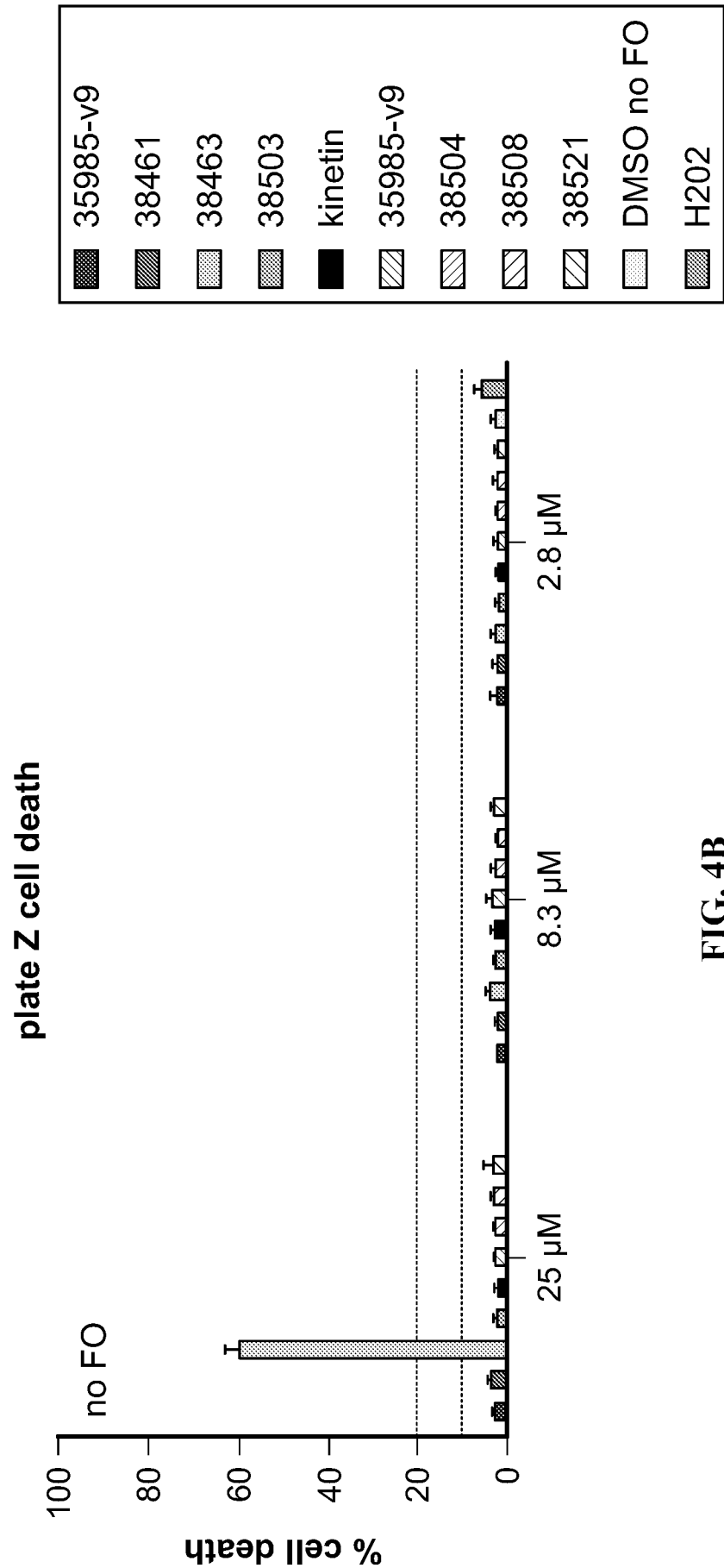


FIG. 4B

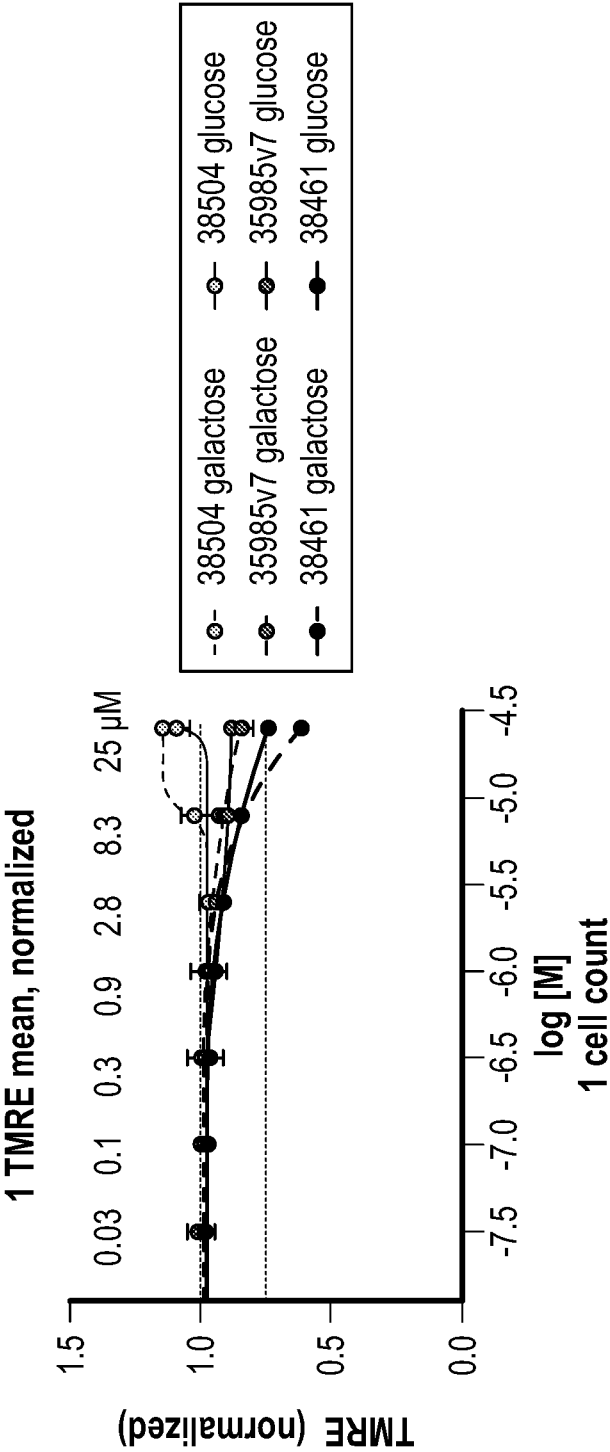


FIG. 5A

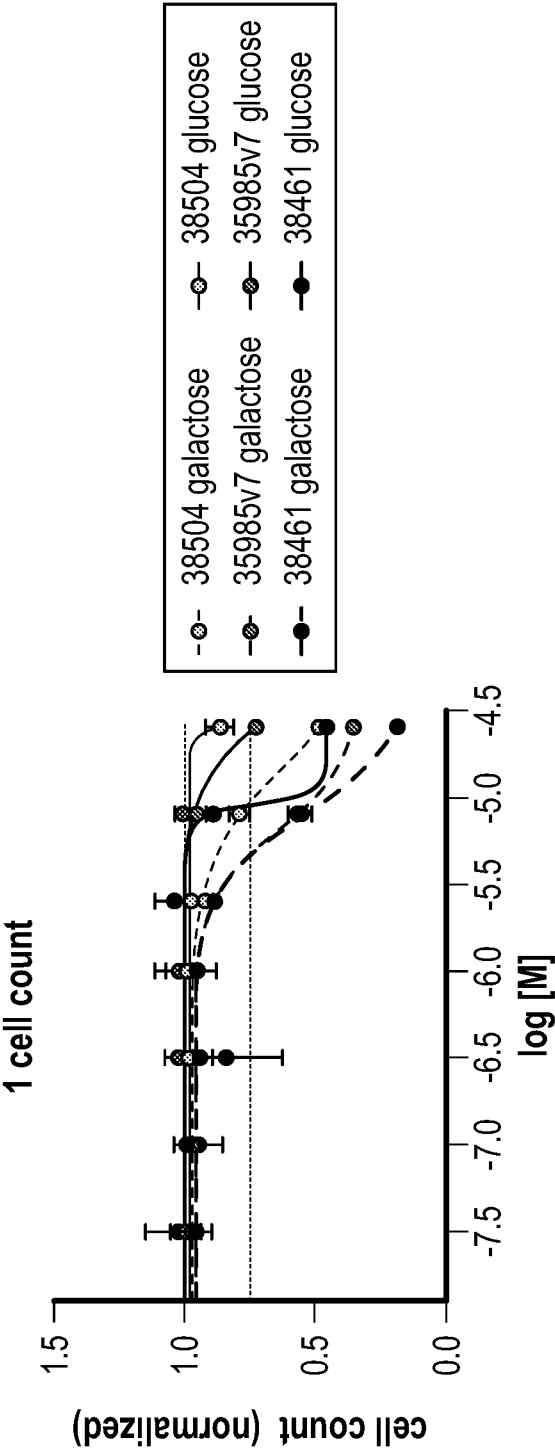


FIG. 5B

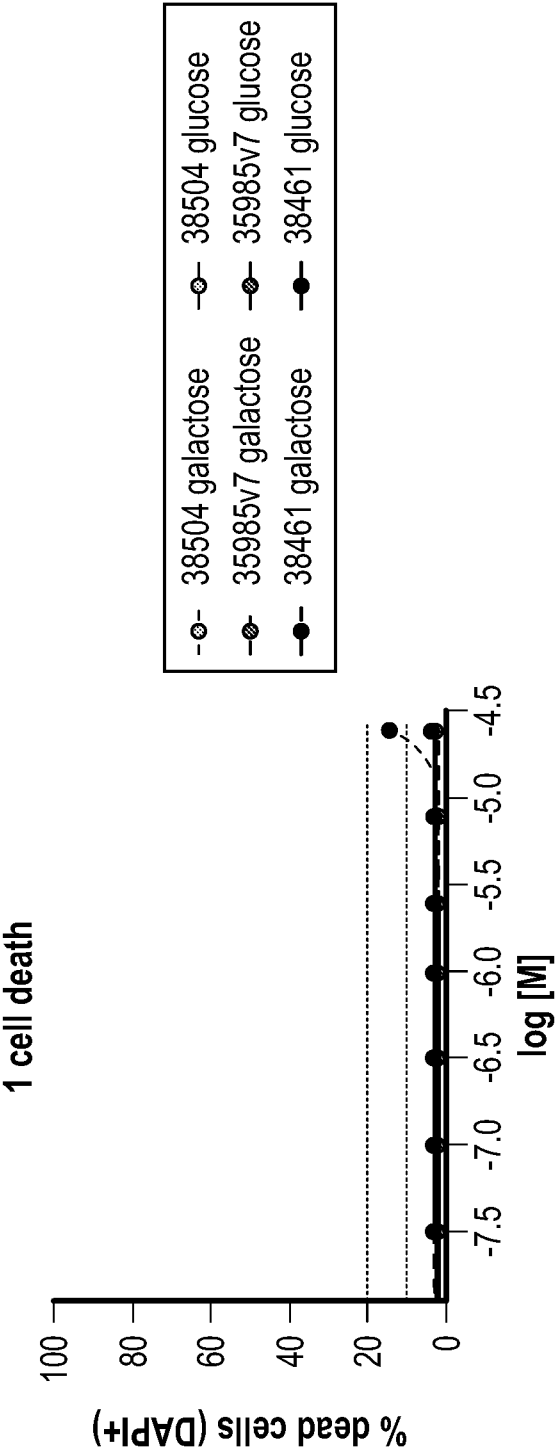


FIG. 5C

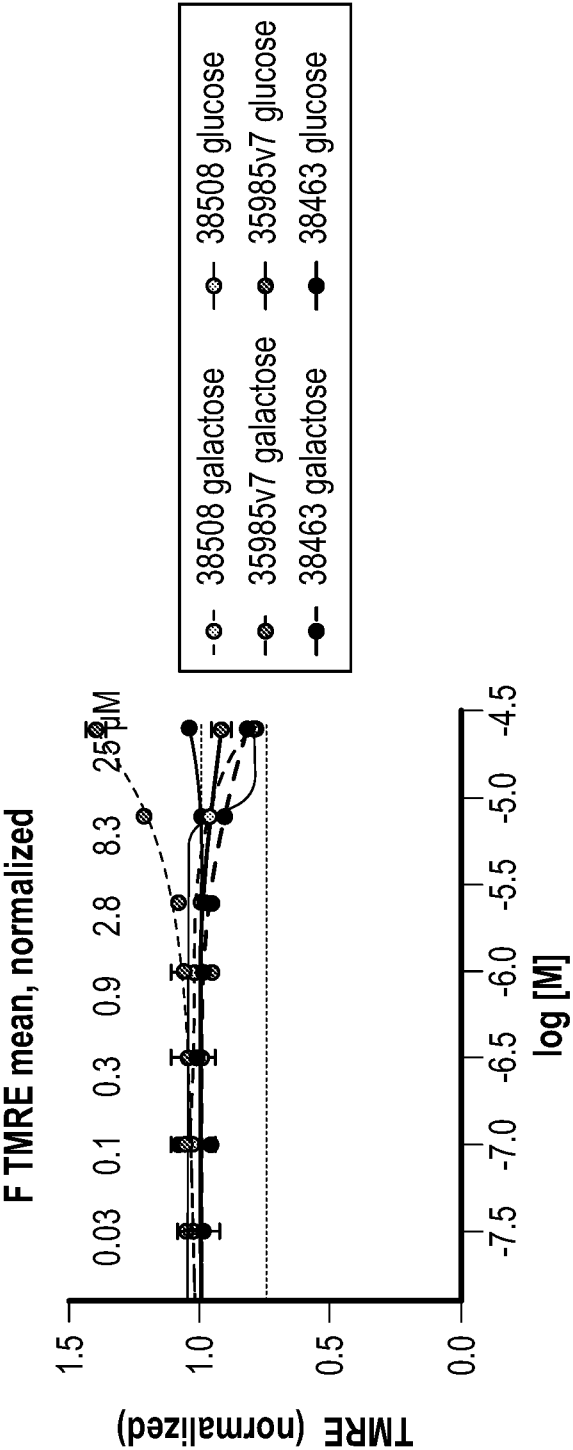


FIG. 6A

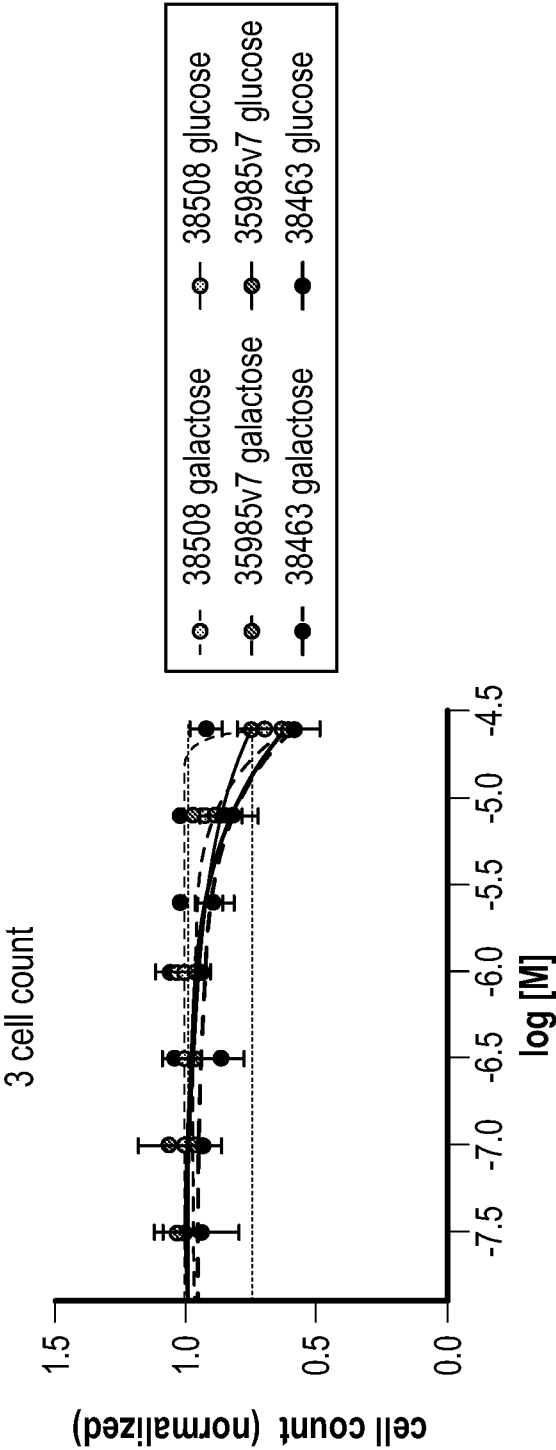


FIG. 6B

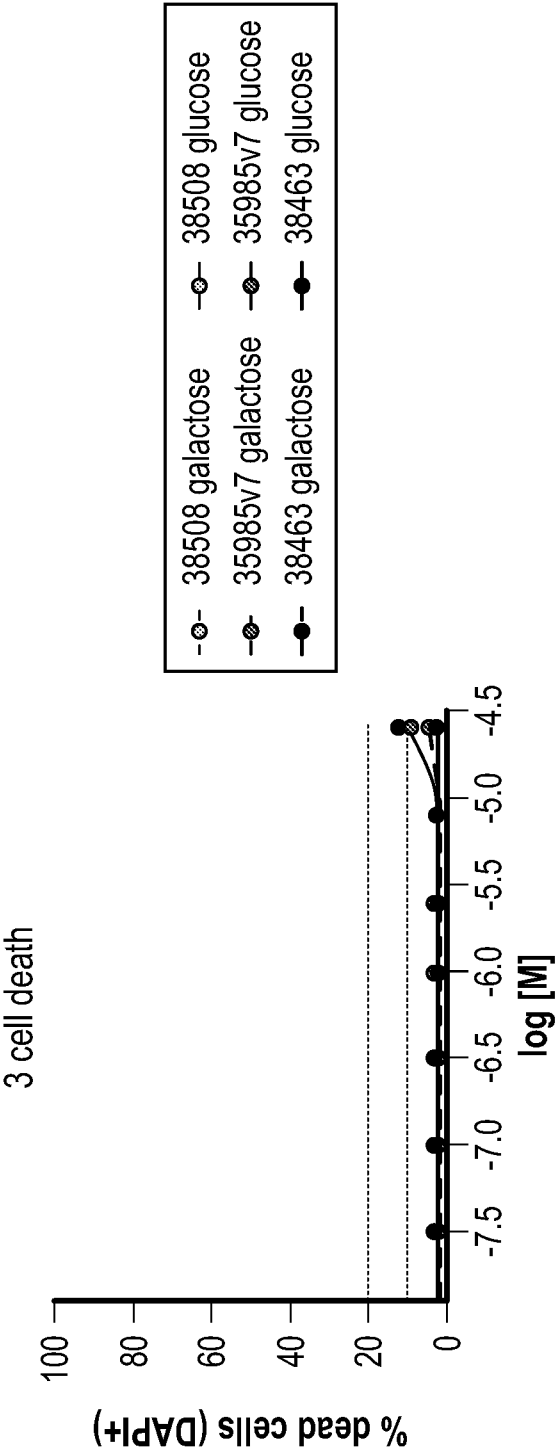


FIG. 6C

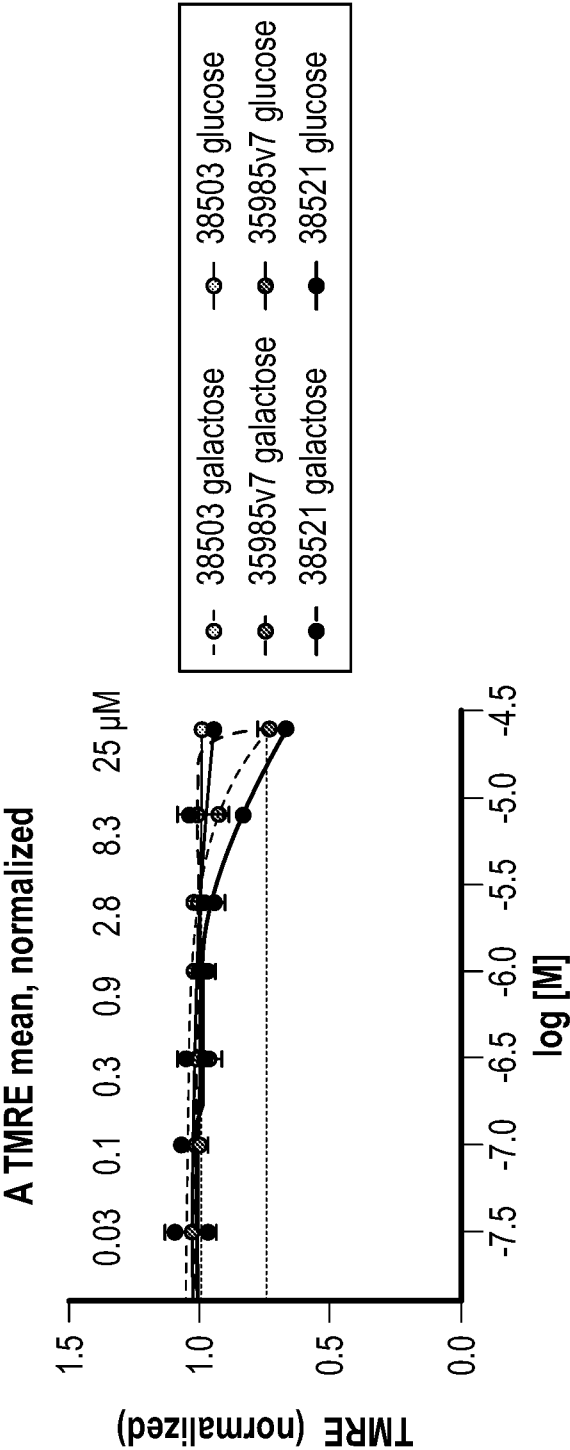


FIG. 7A

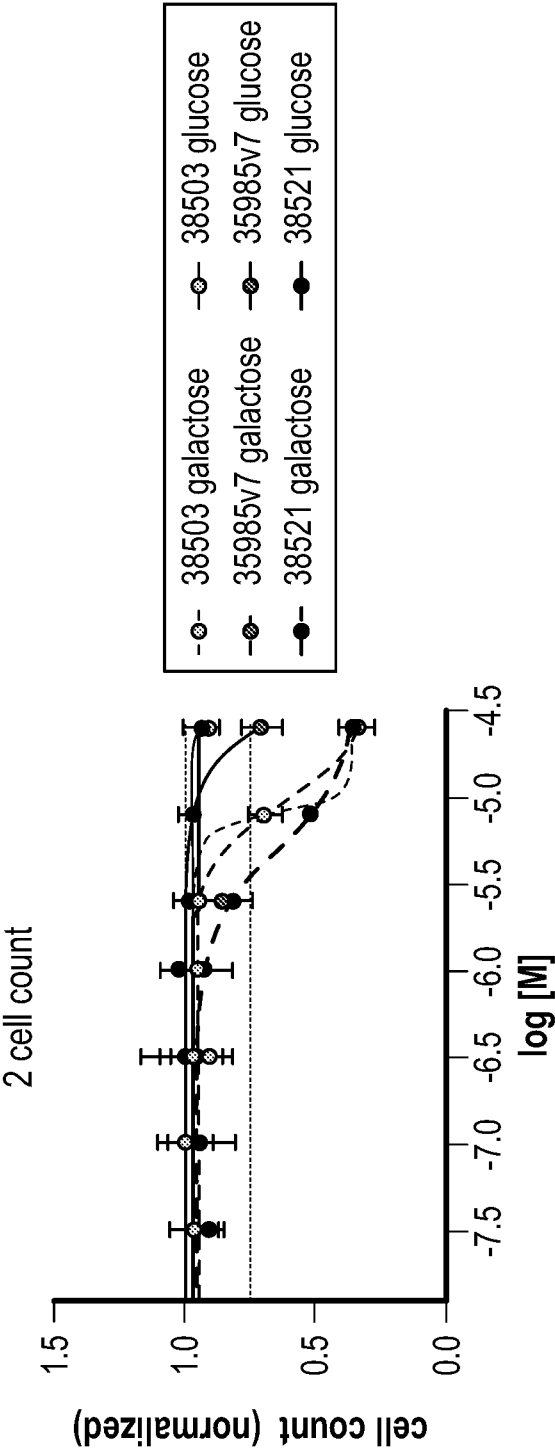


FIG. 7B

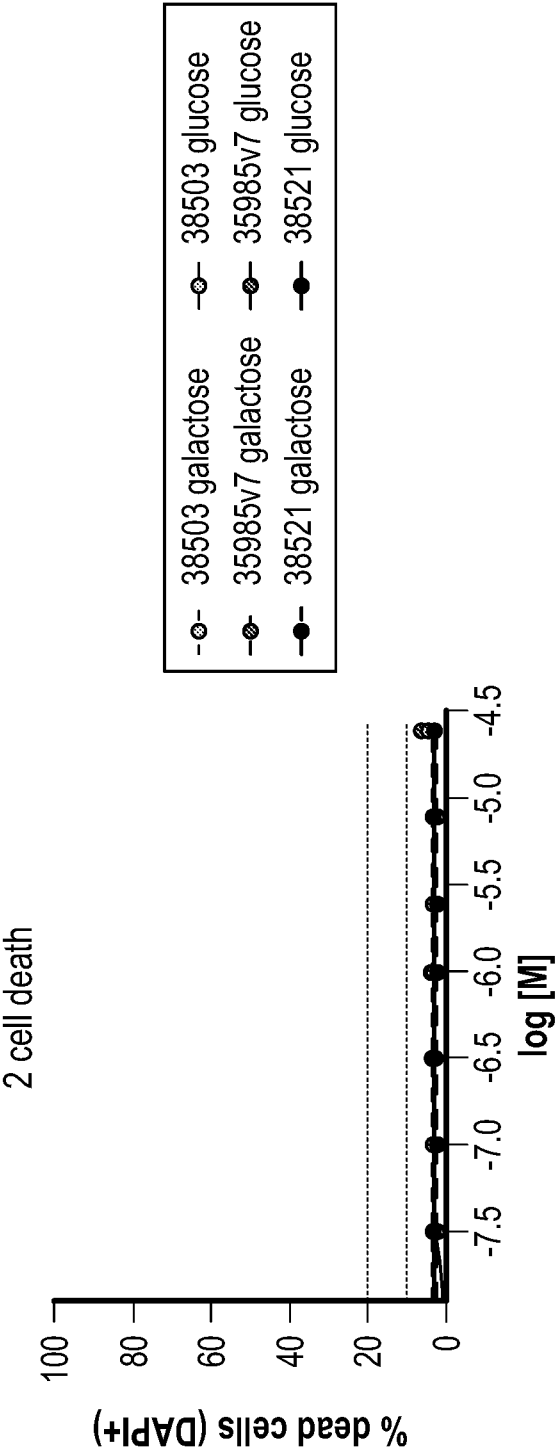


FIG. 7C

27/80

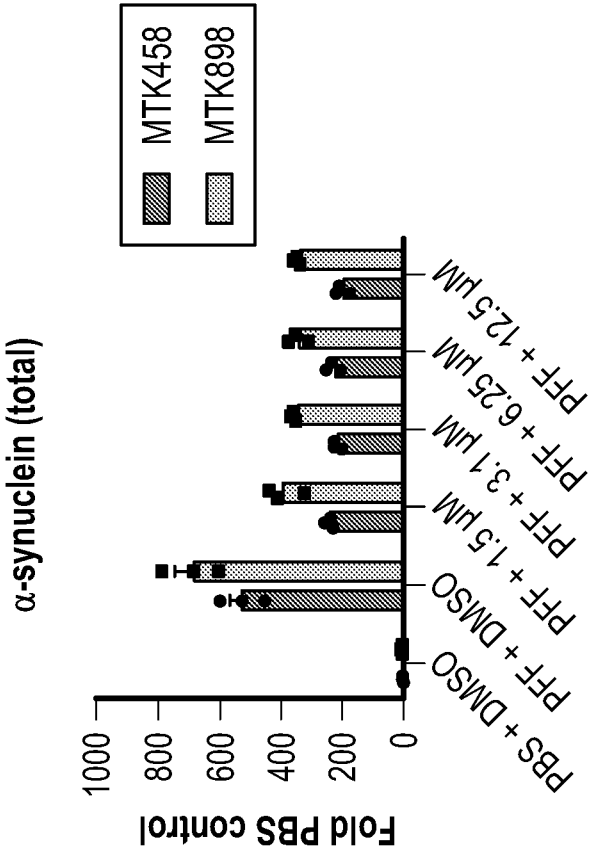


FIG. 8C

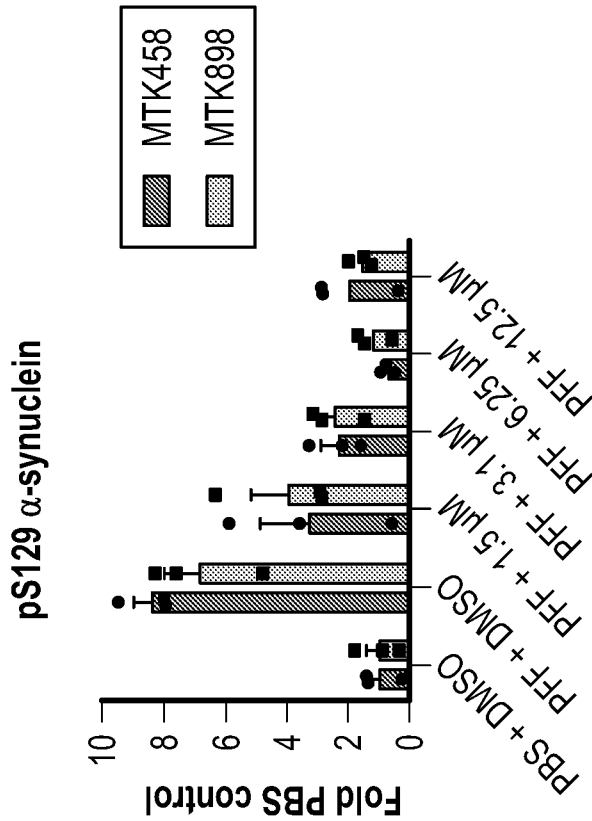
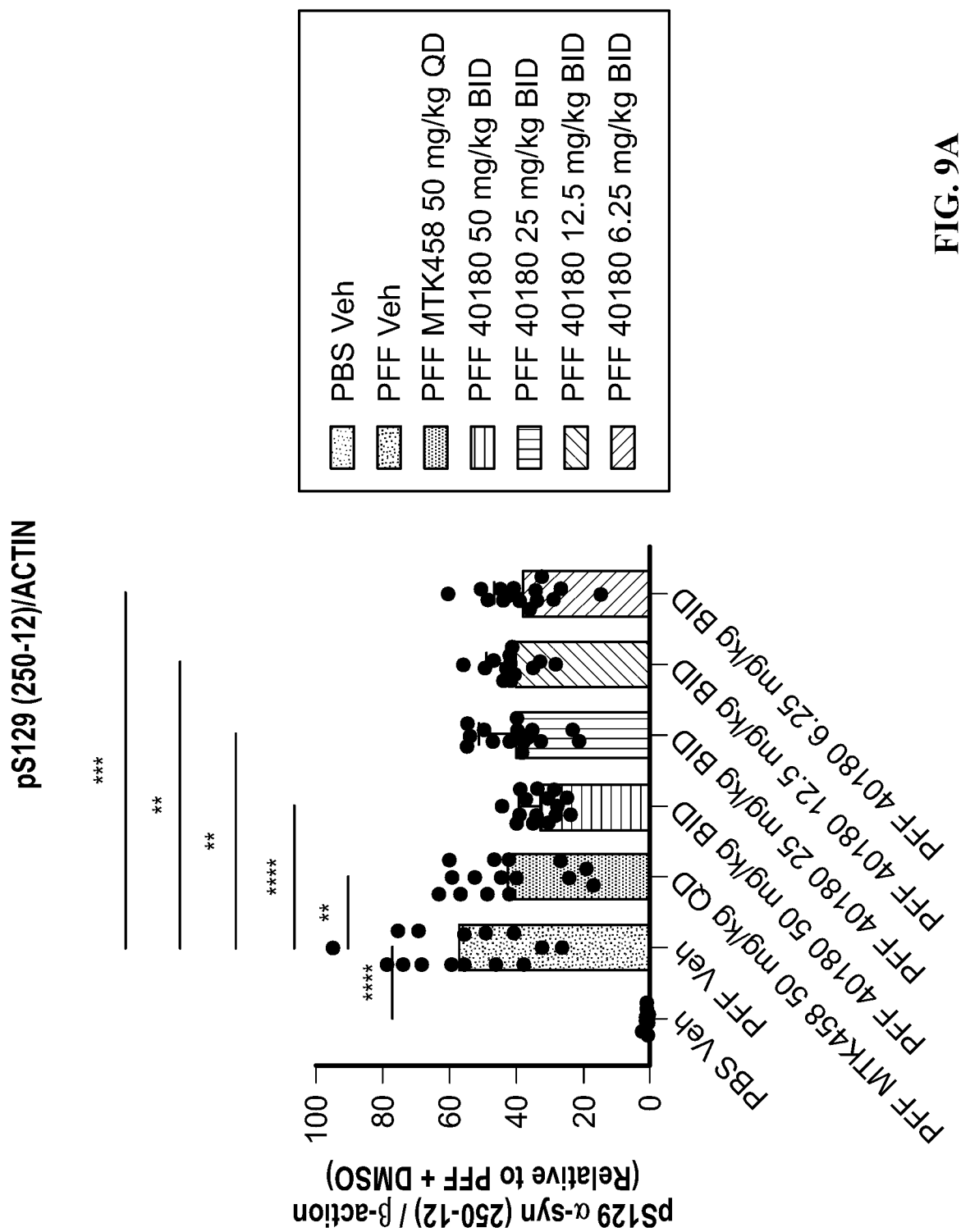
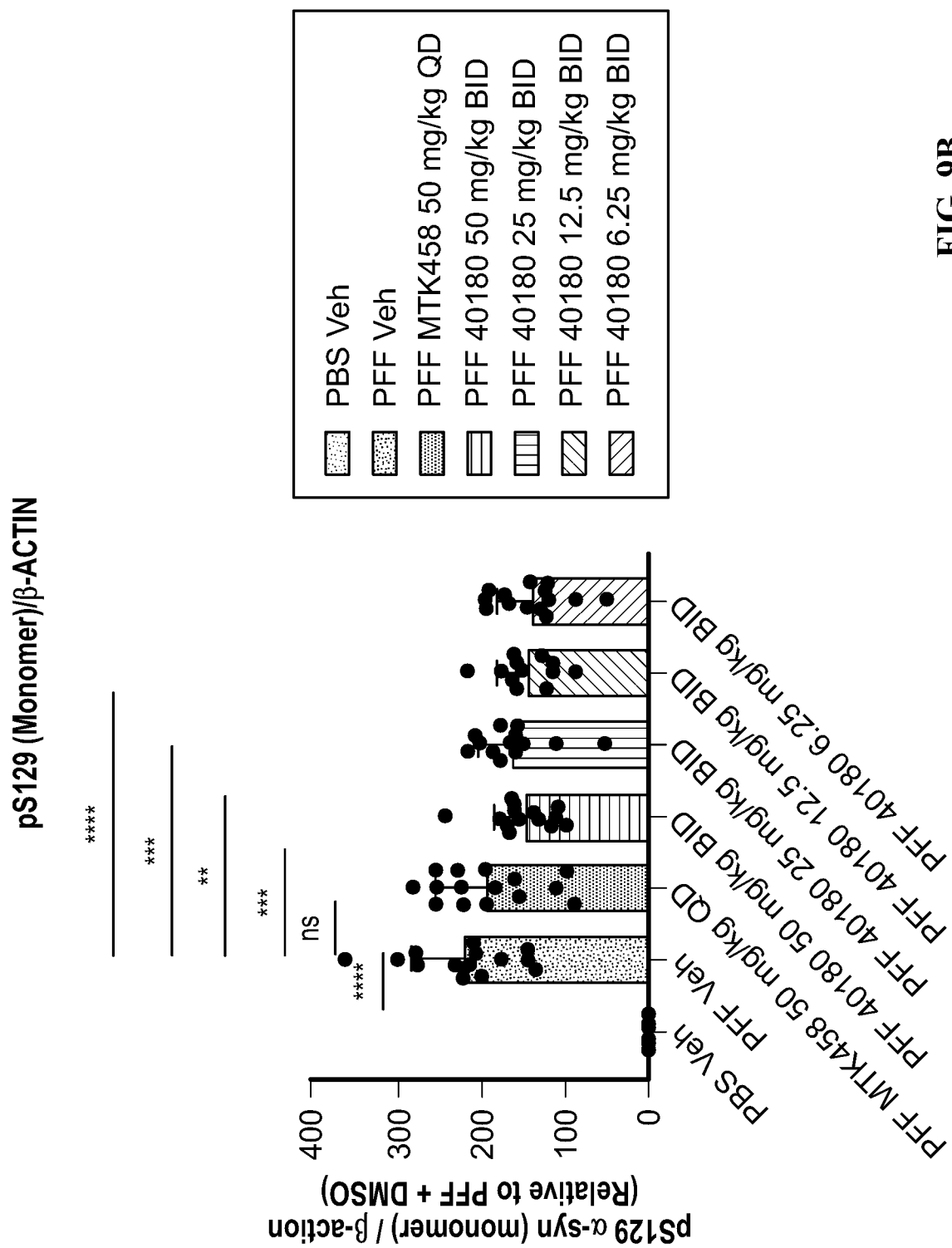


FIG. 8B





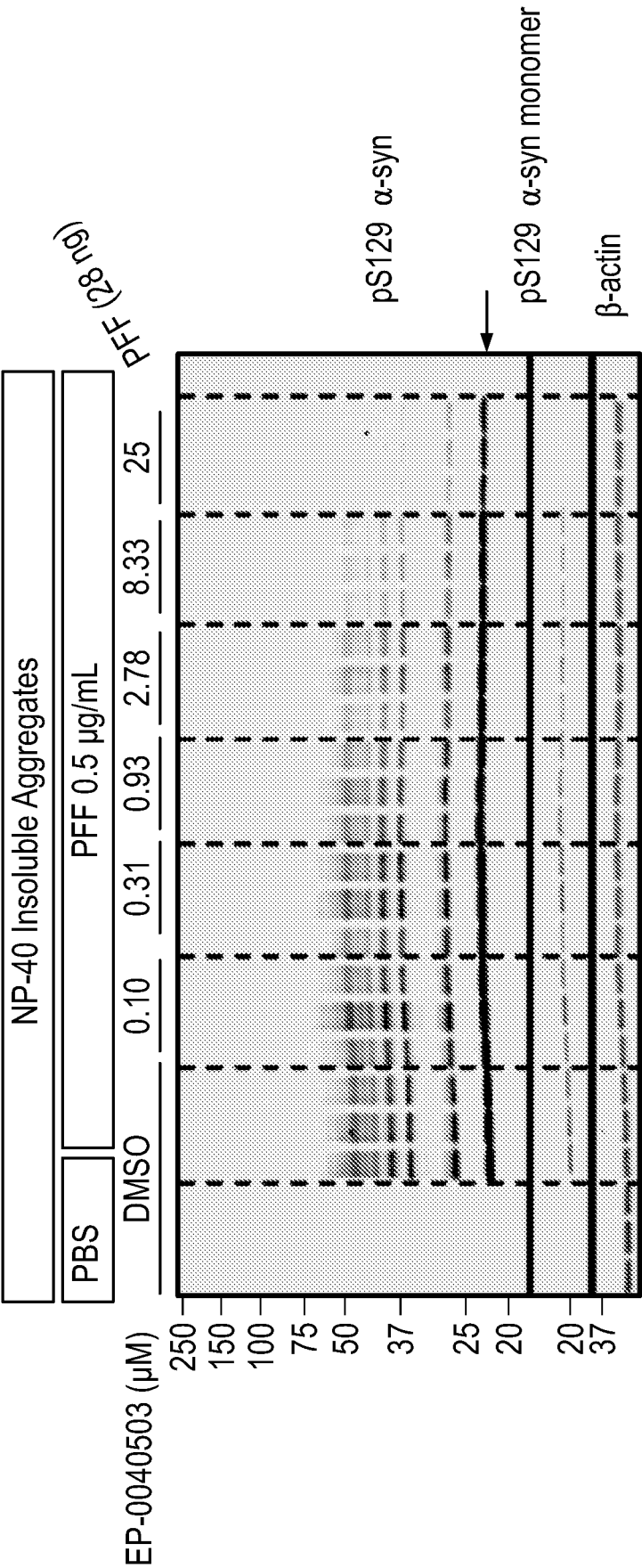


FIG. 10A

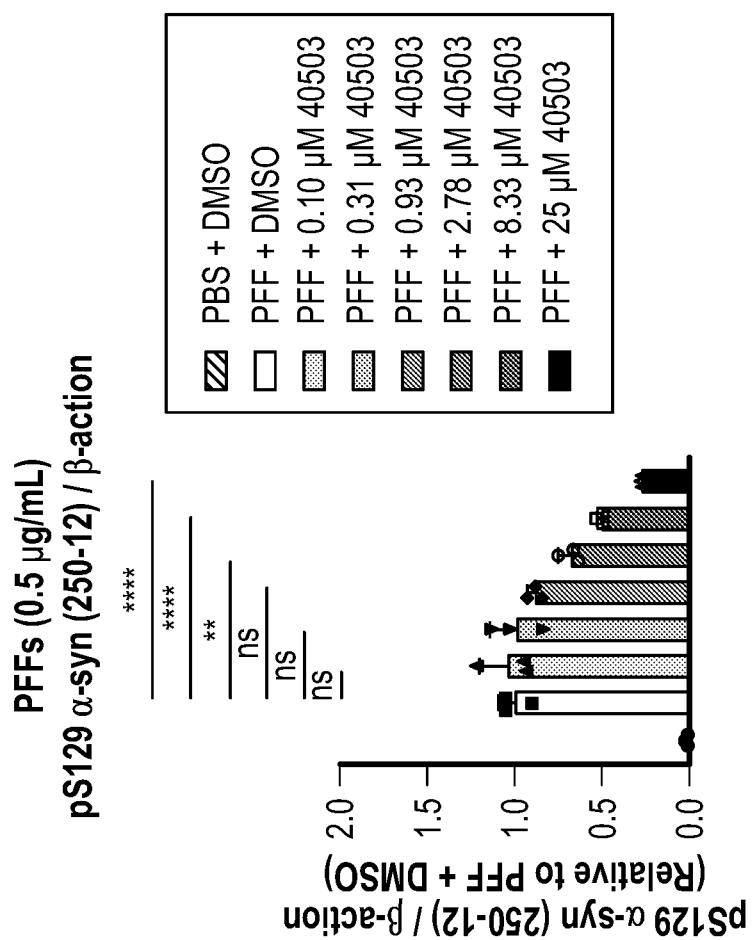


FIG. 10B

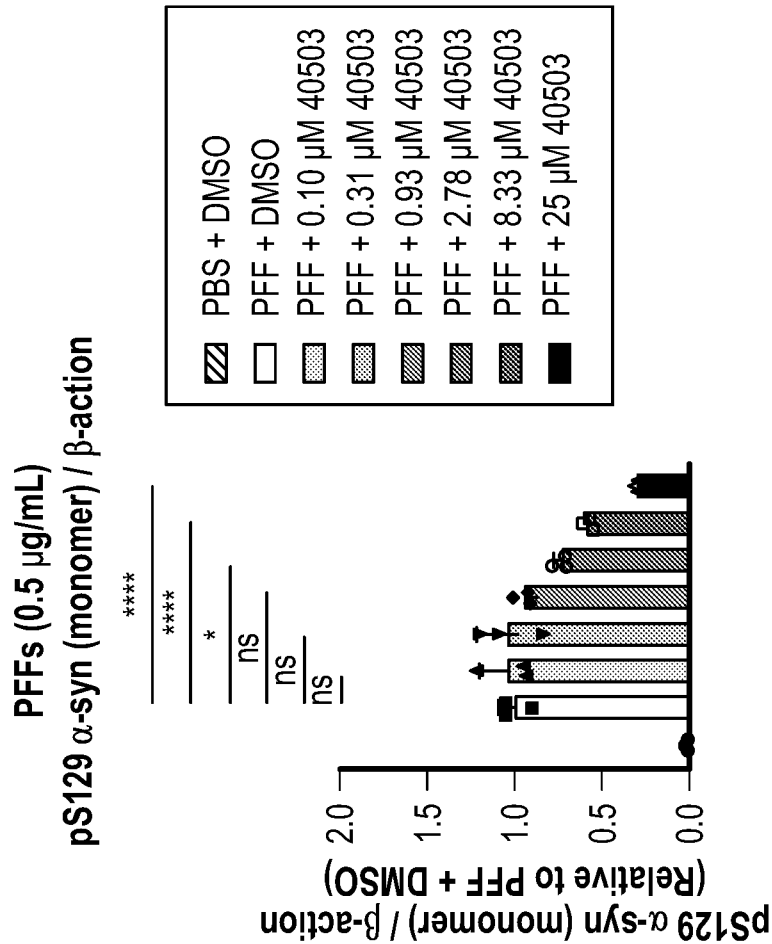


FIG. 10C

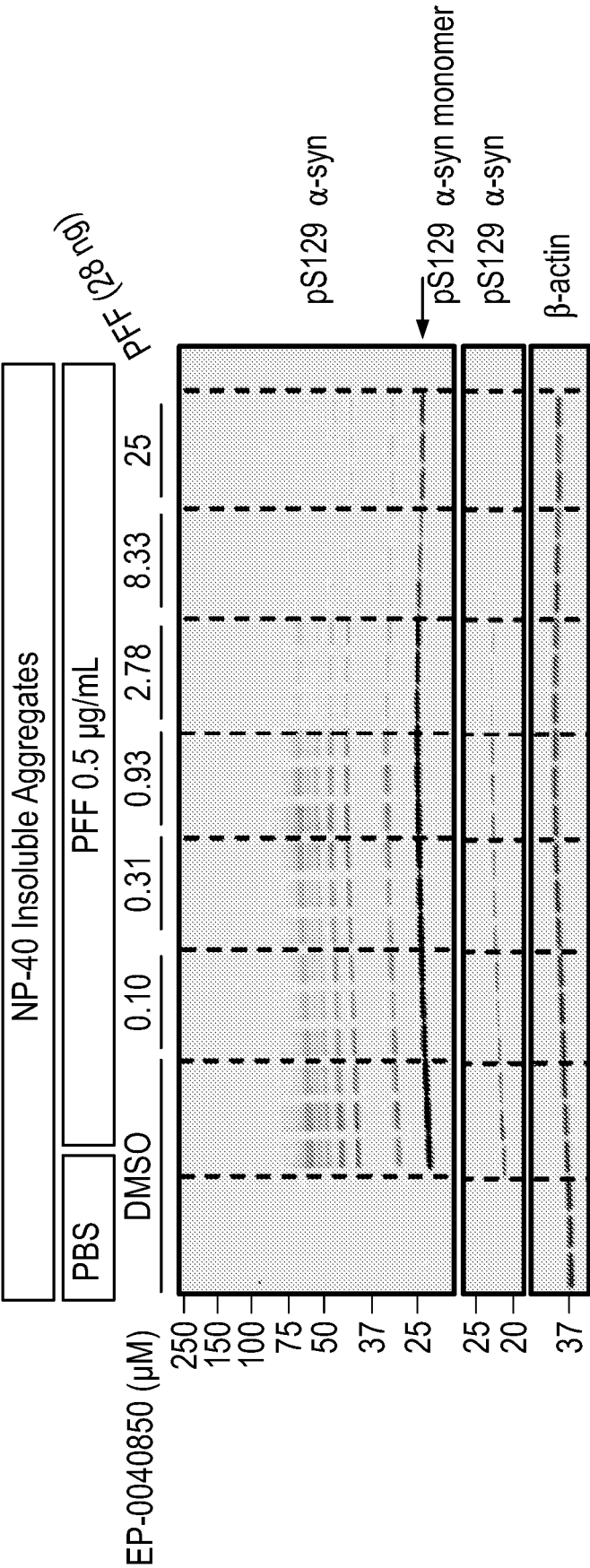


FIG. 11A

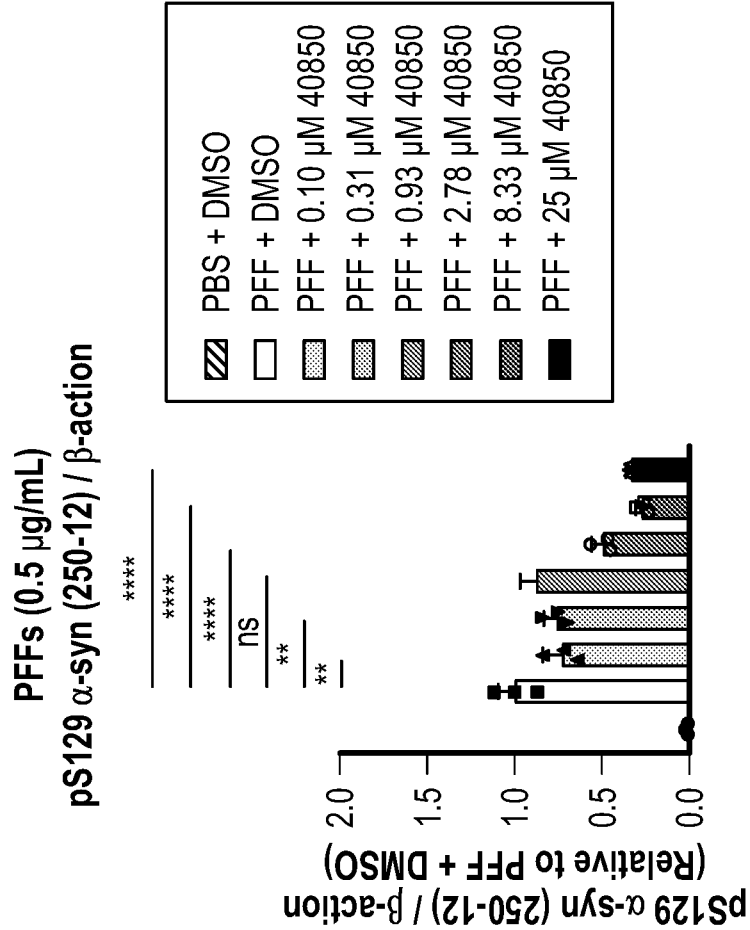


FIG. 11B

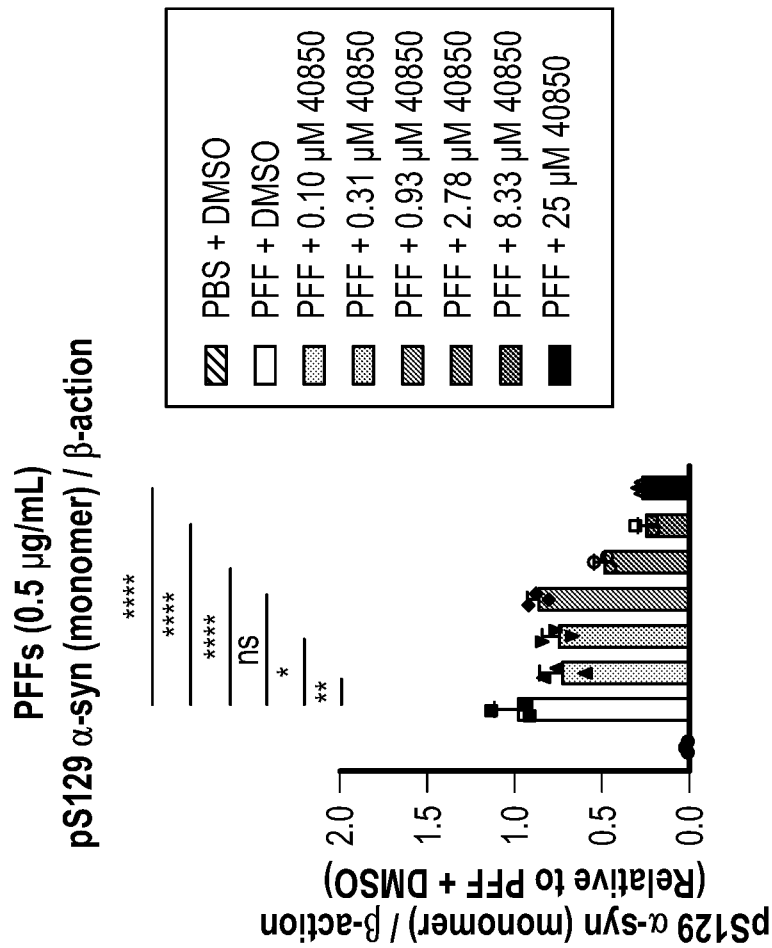


FIG. 11C

36/80

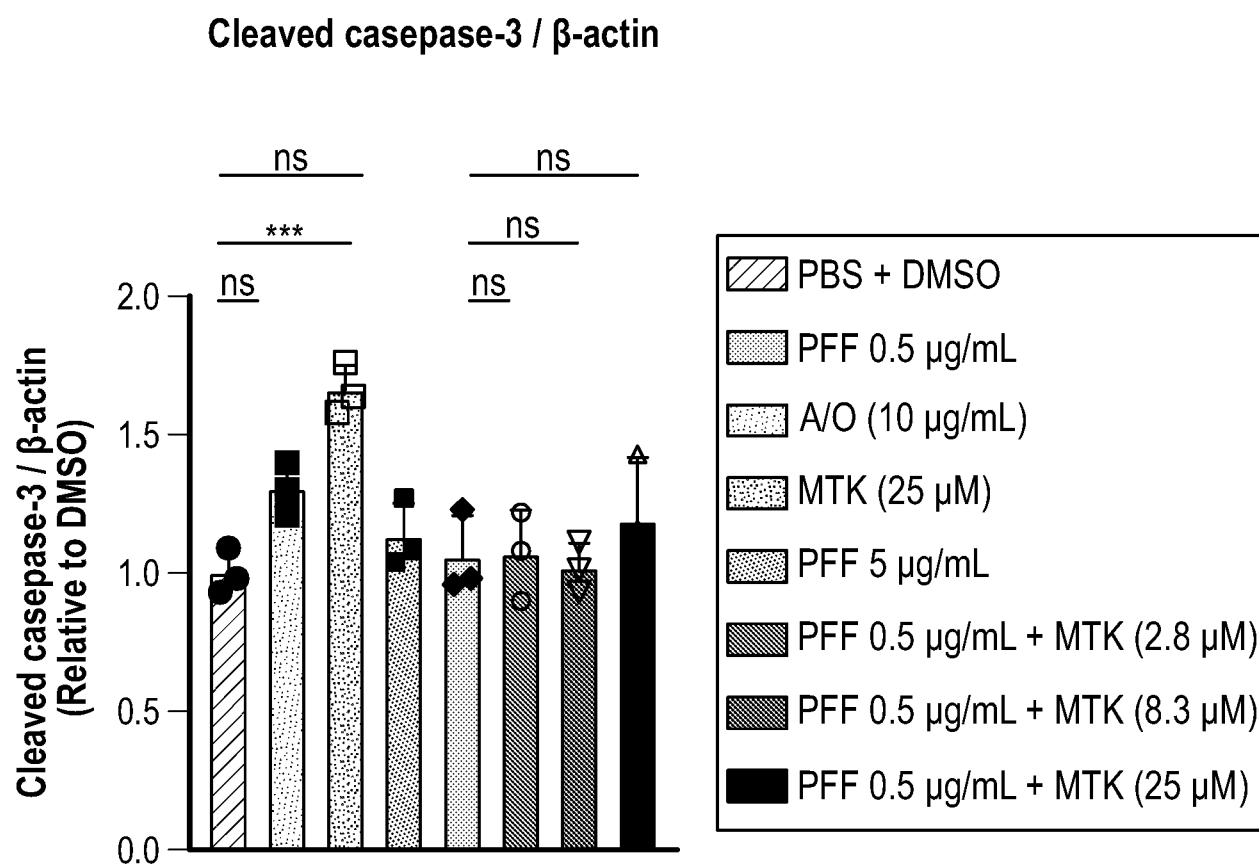


FIG. 12

37/80

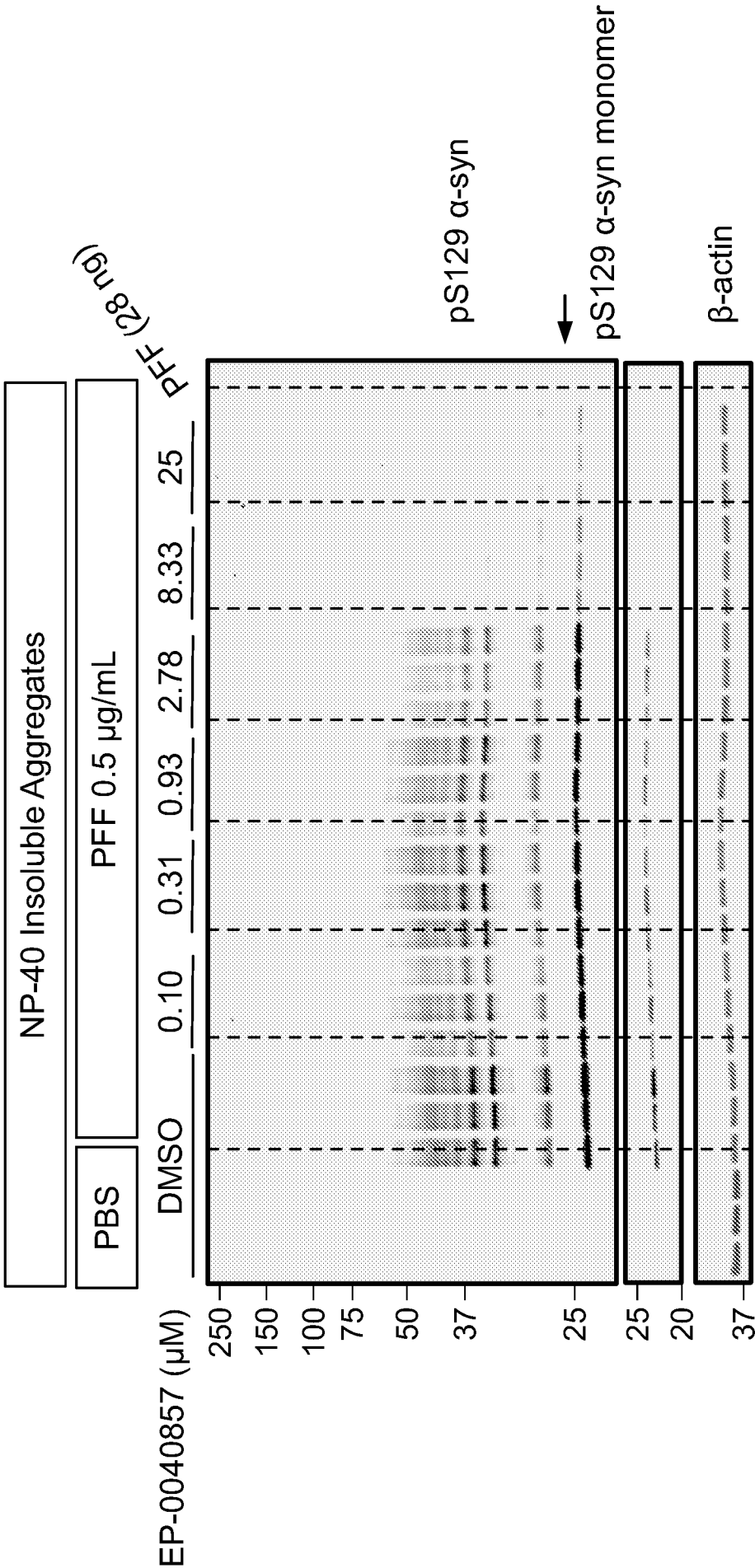


FIG. 13A

38/80

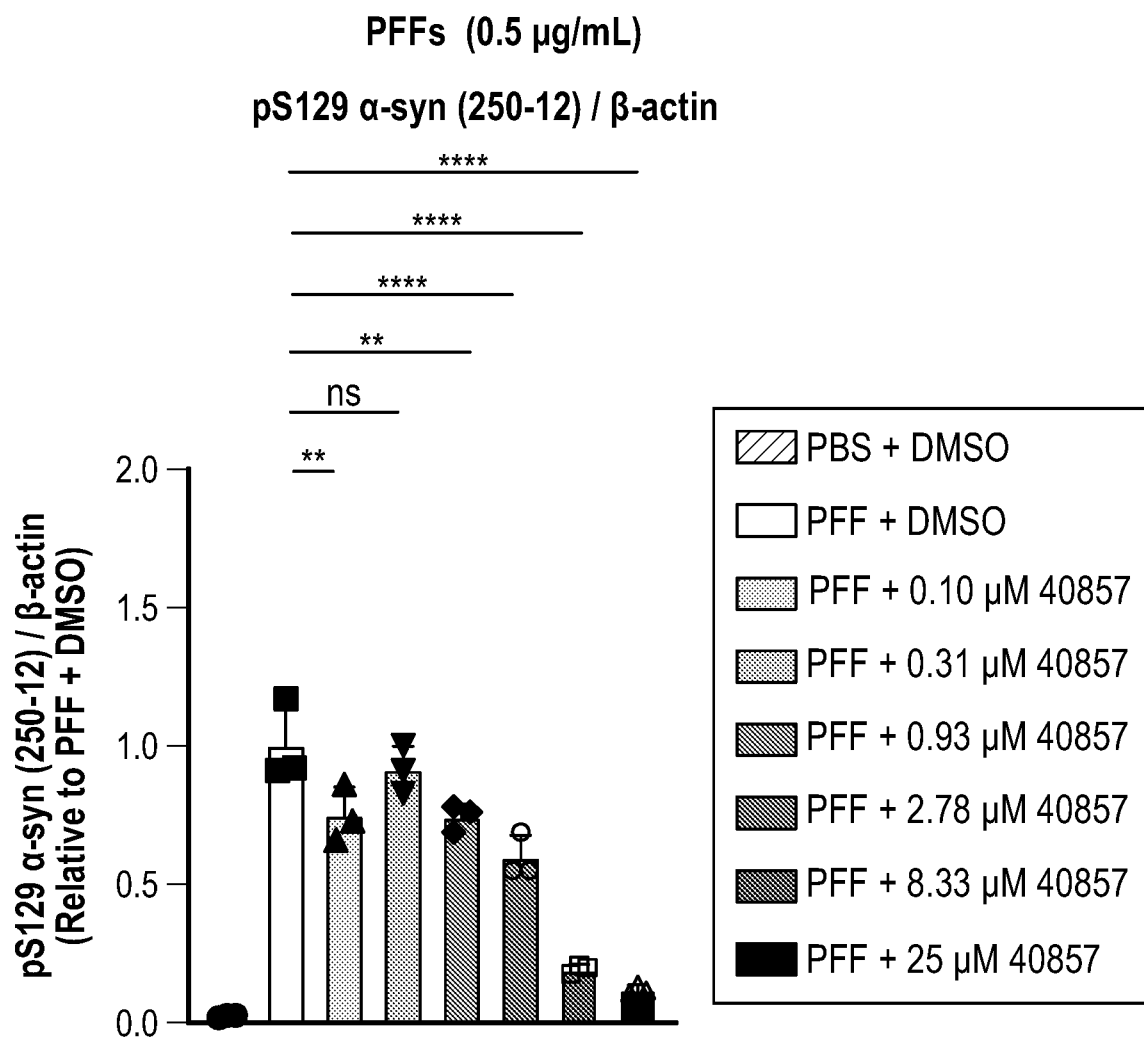


FIG. 13B

39/80

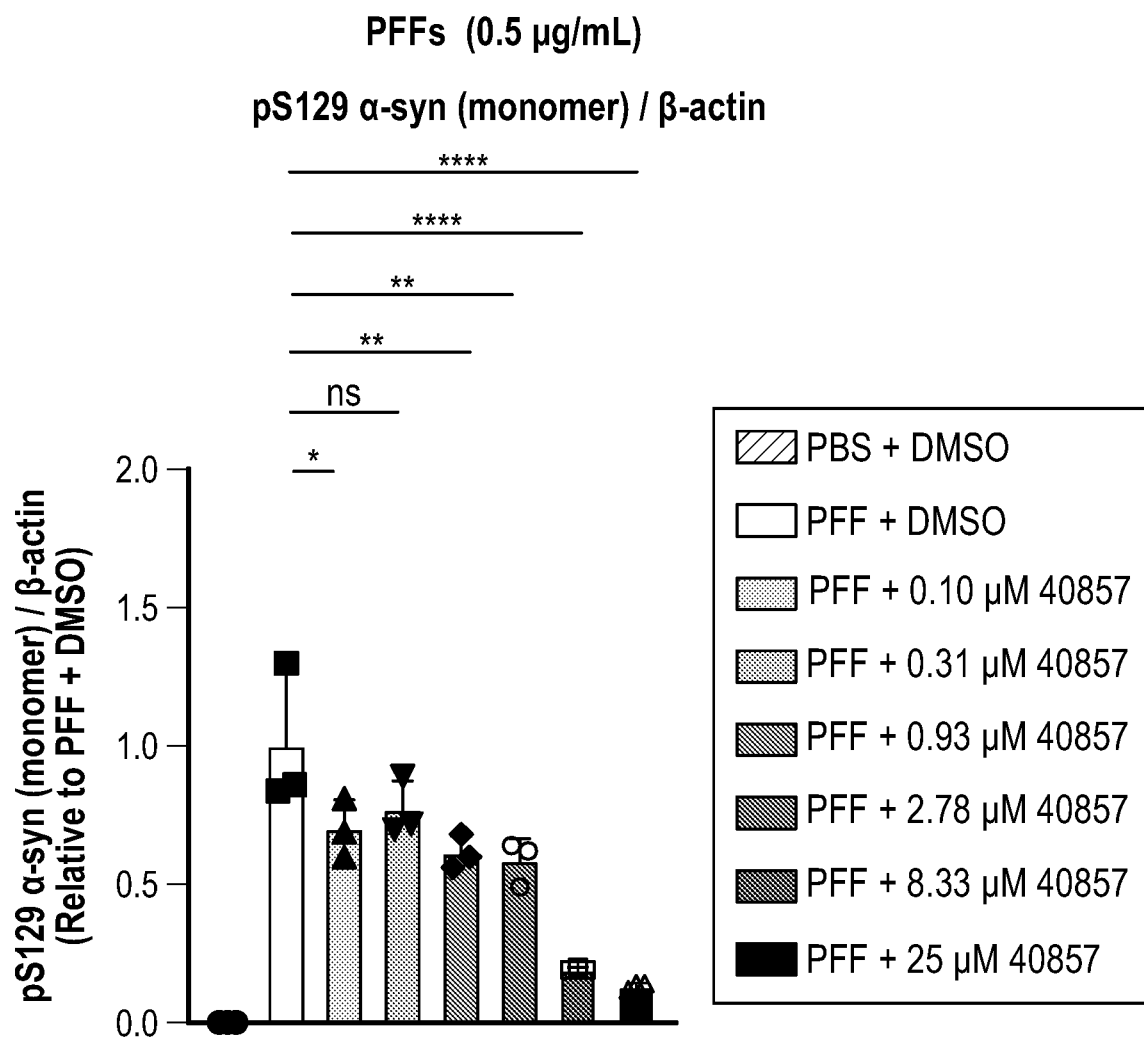


FIG. 13C

40/80

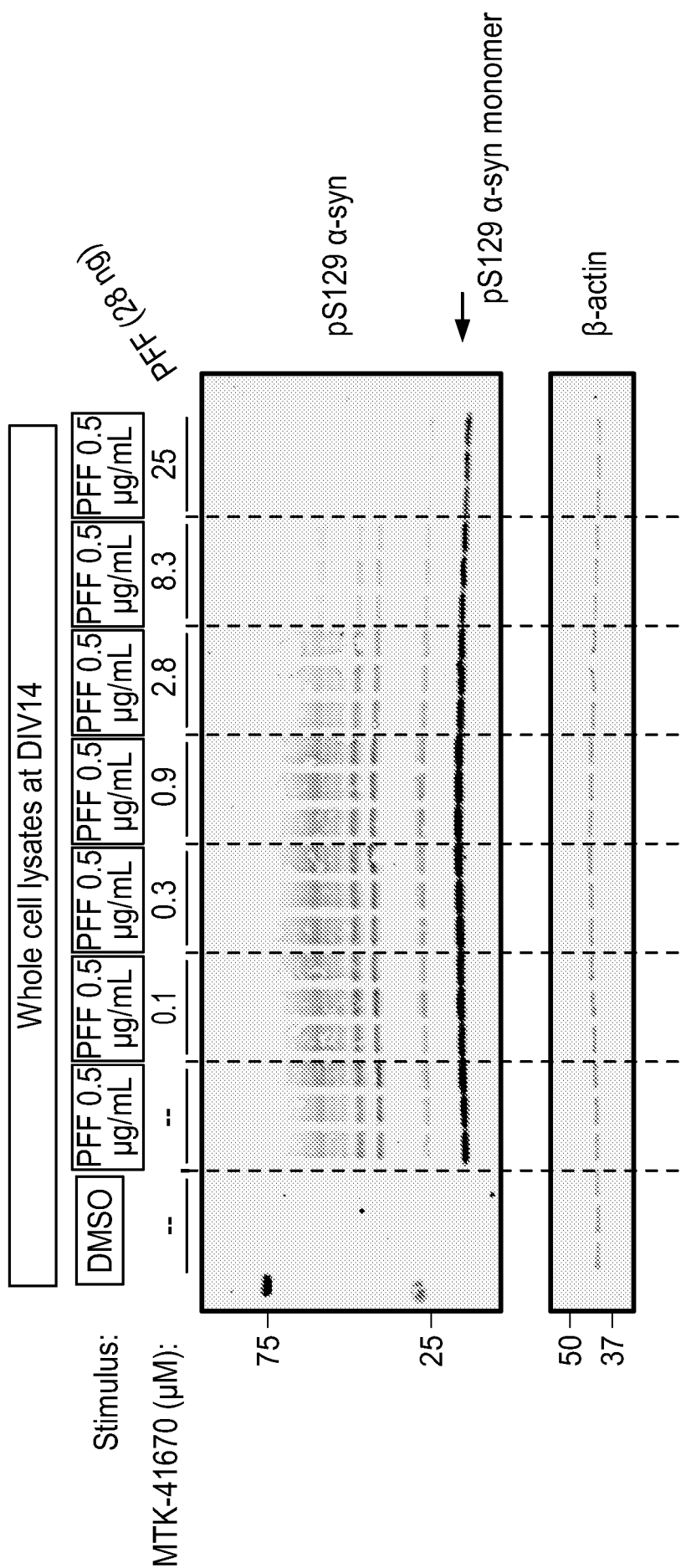


FIG. 14A

41/80

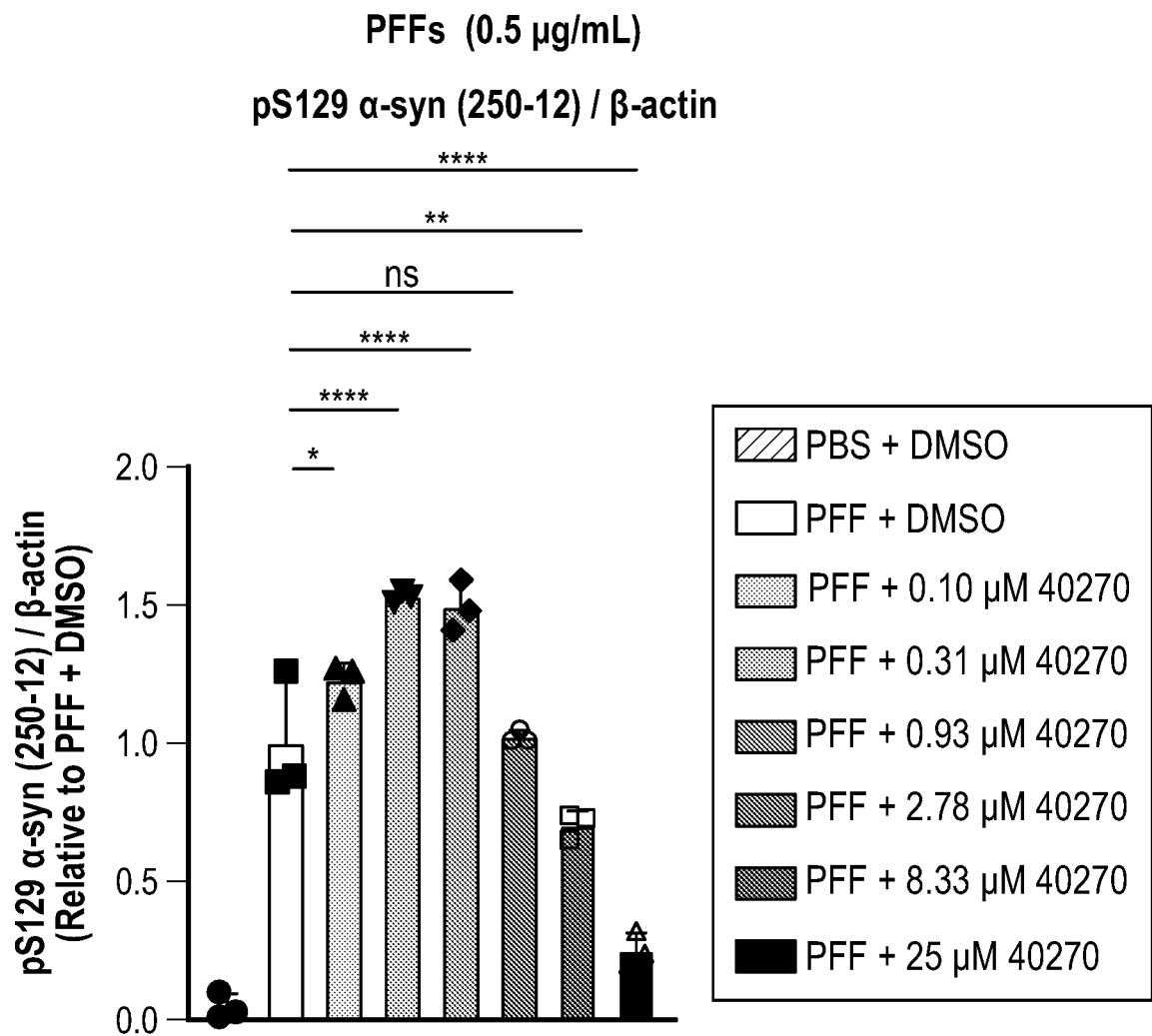


FIG. 14B

42/80

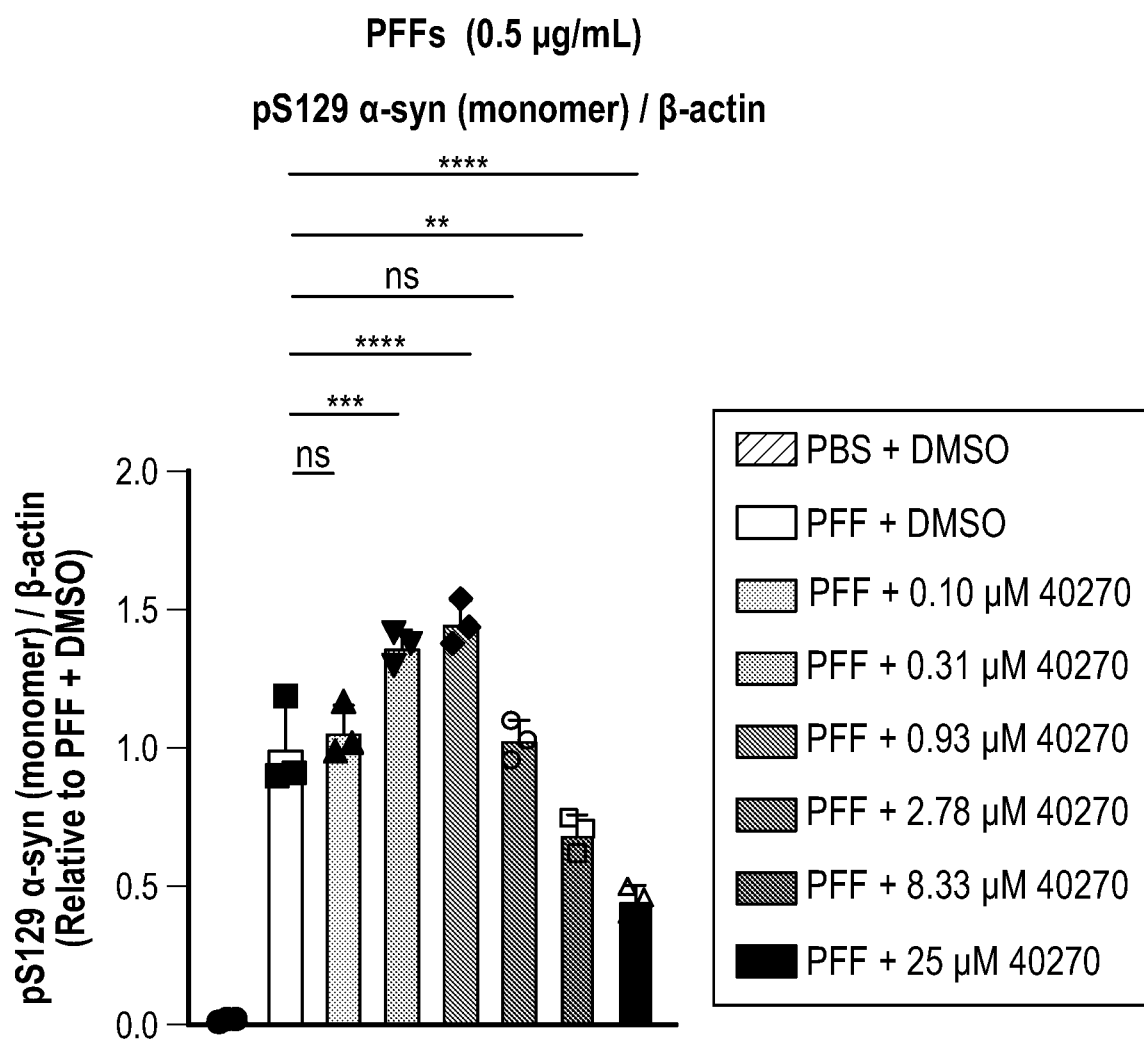


FIG. 14C

43/80

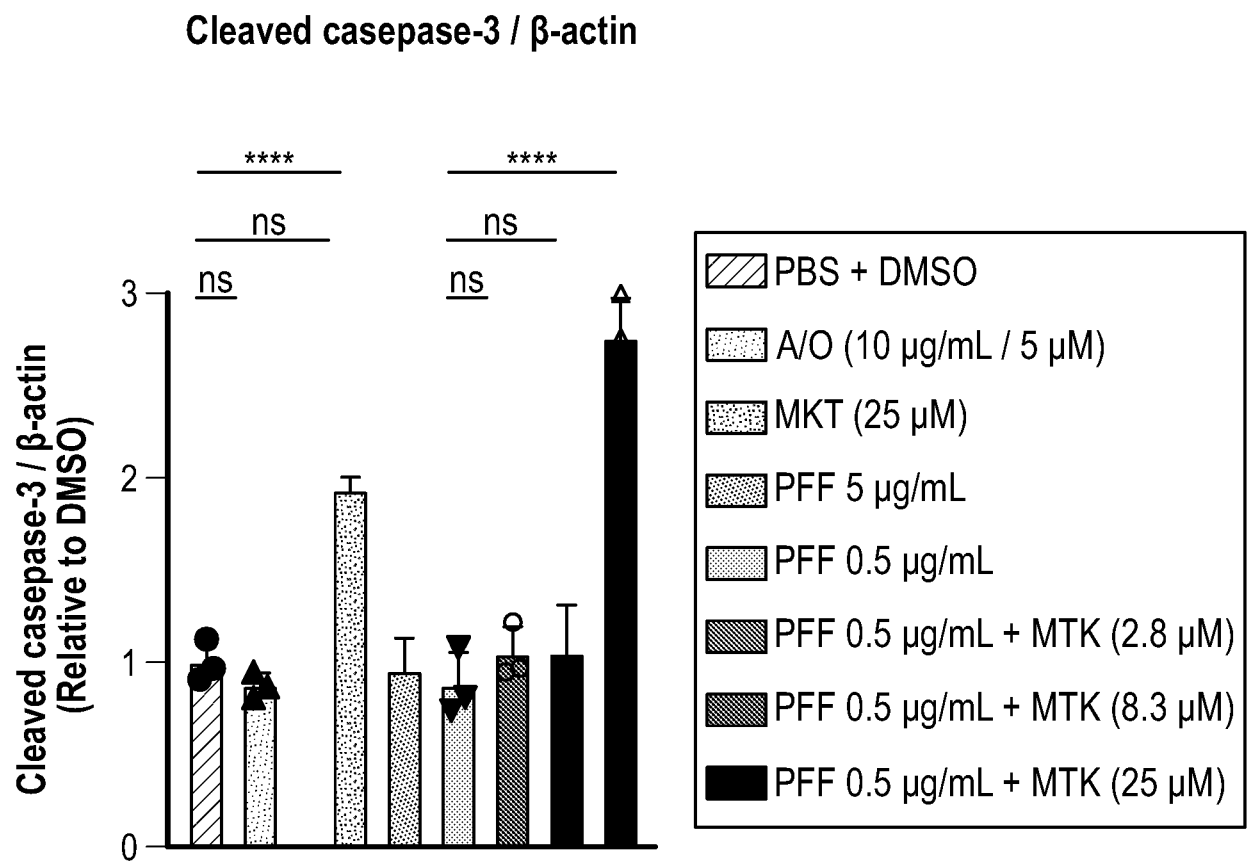
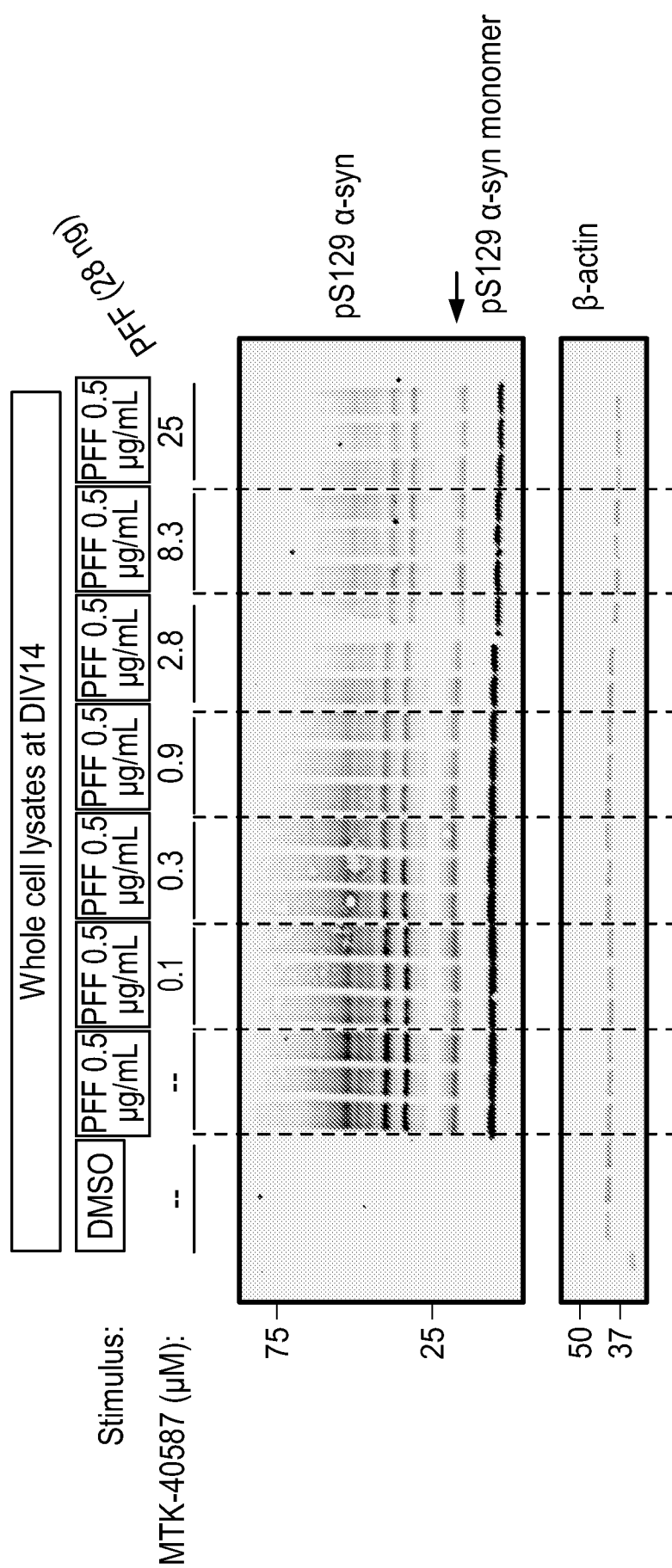


FIG. 15



45/80

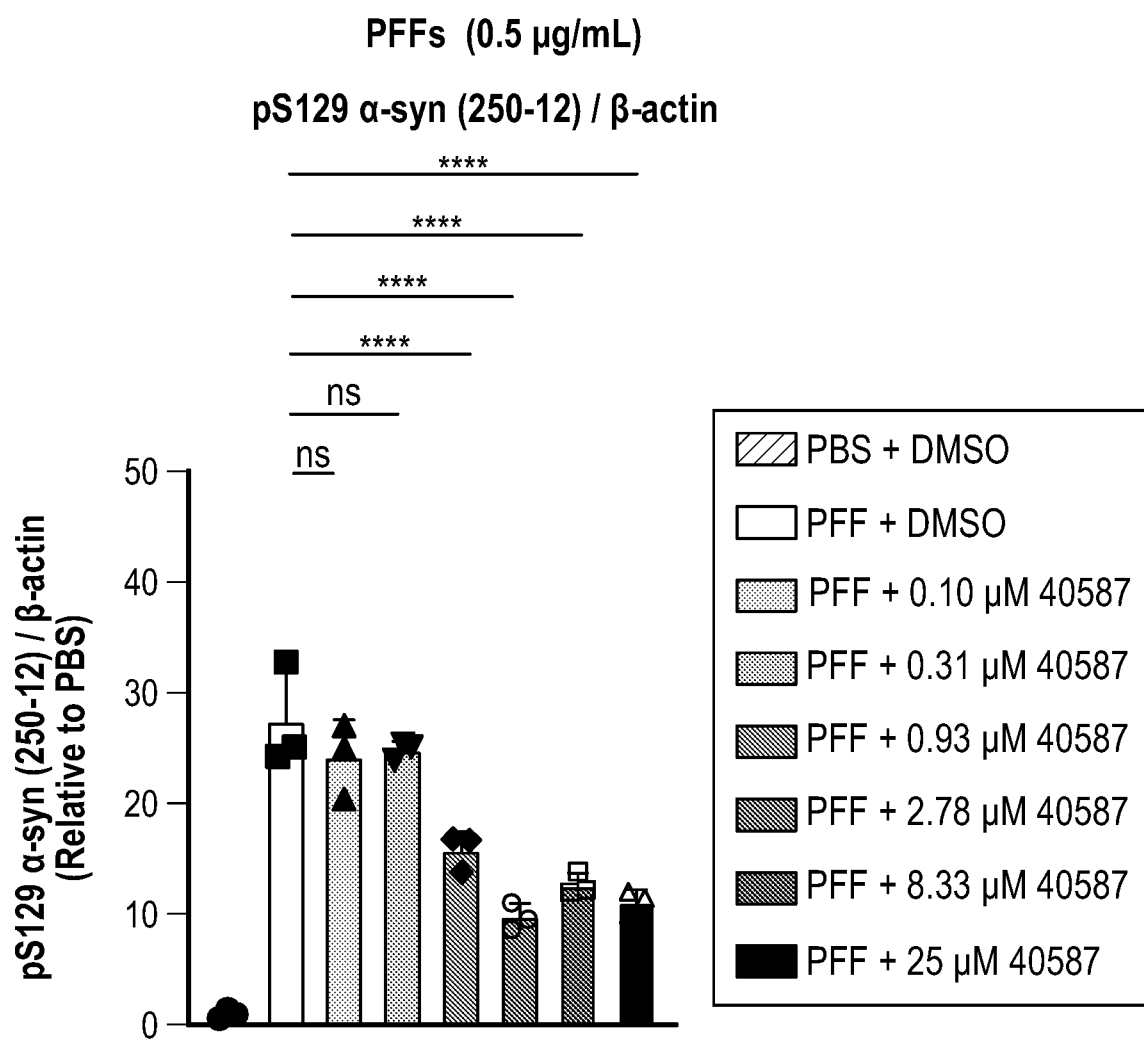


FIG. 16B

46/80

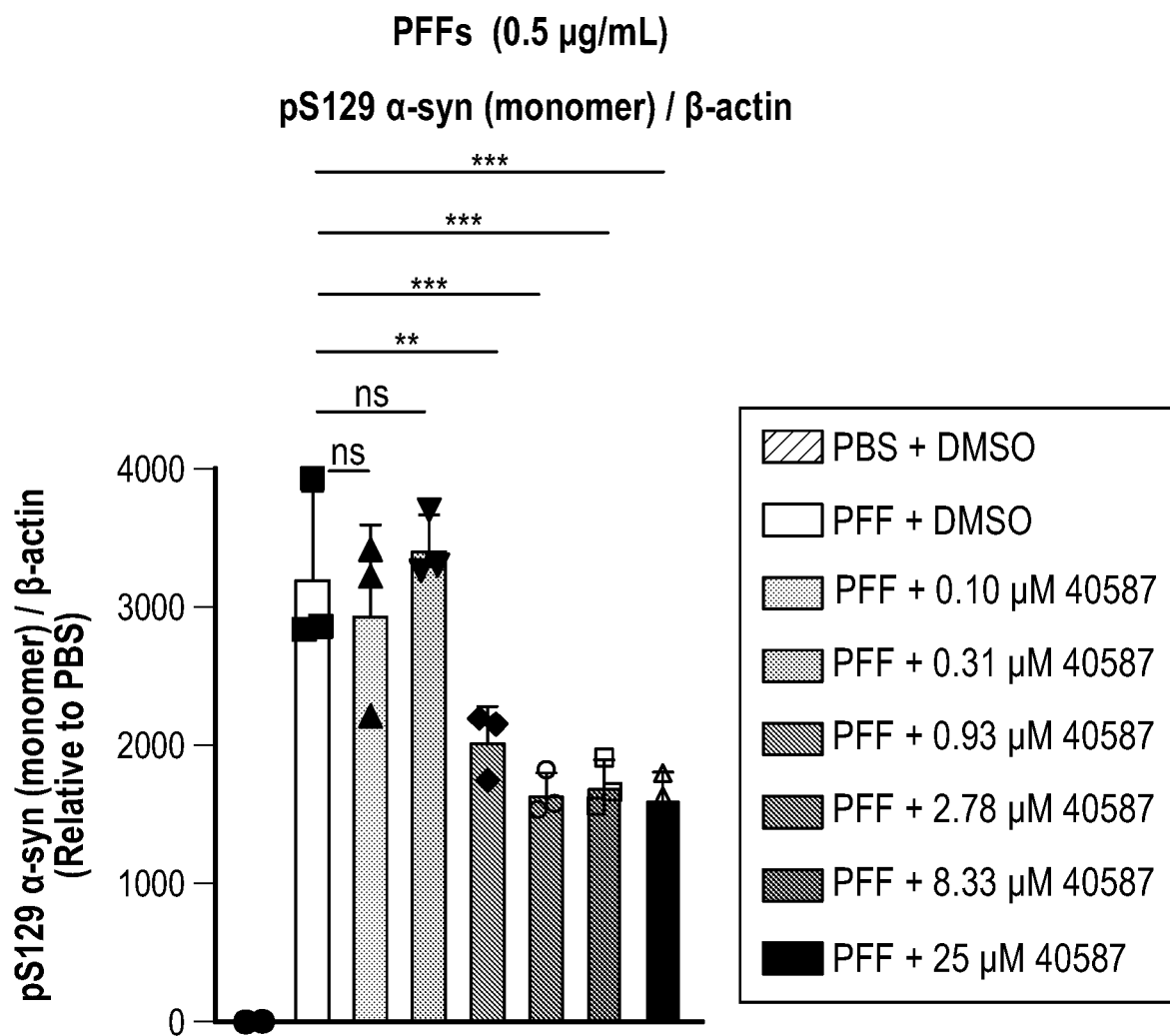


FIG. 16C

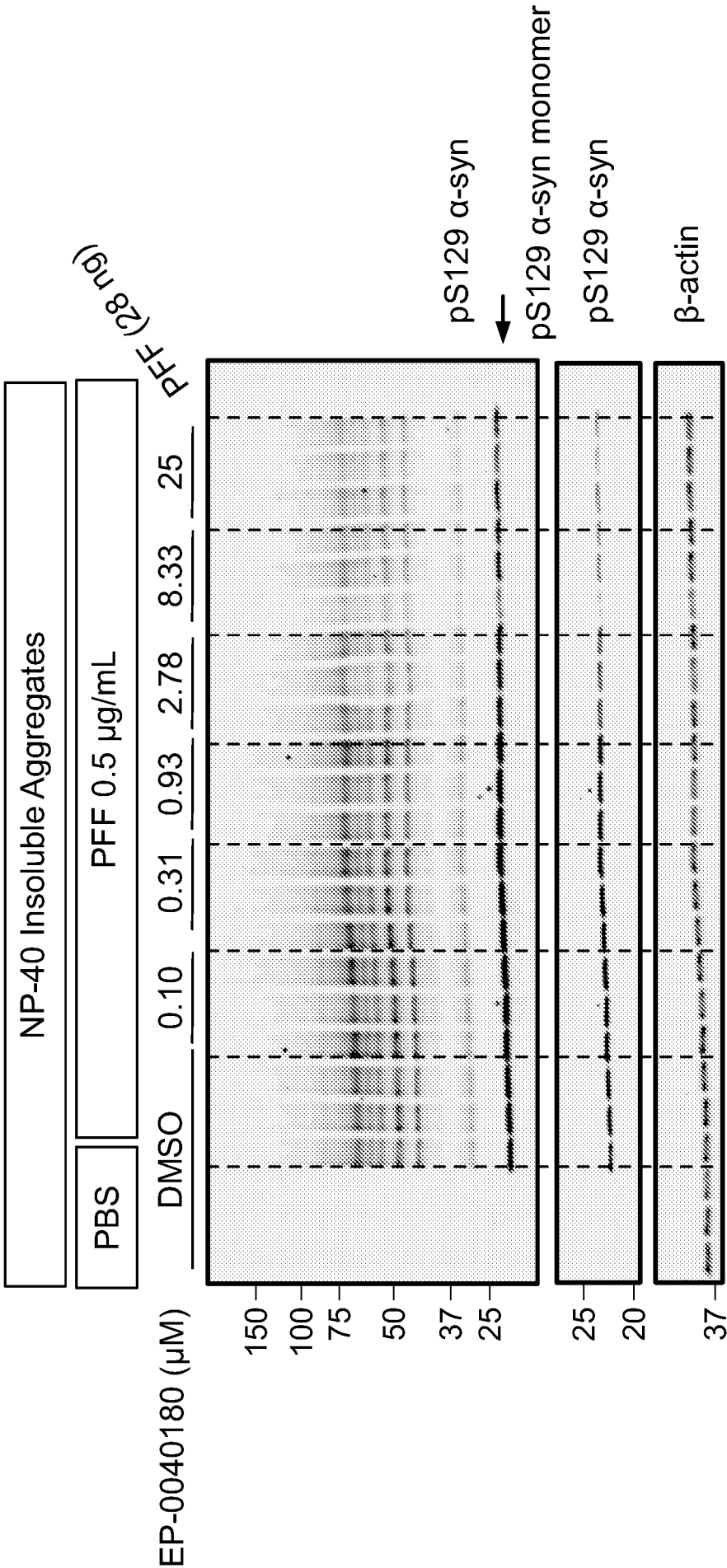


FIG. 17A

48/80

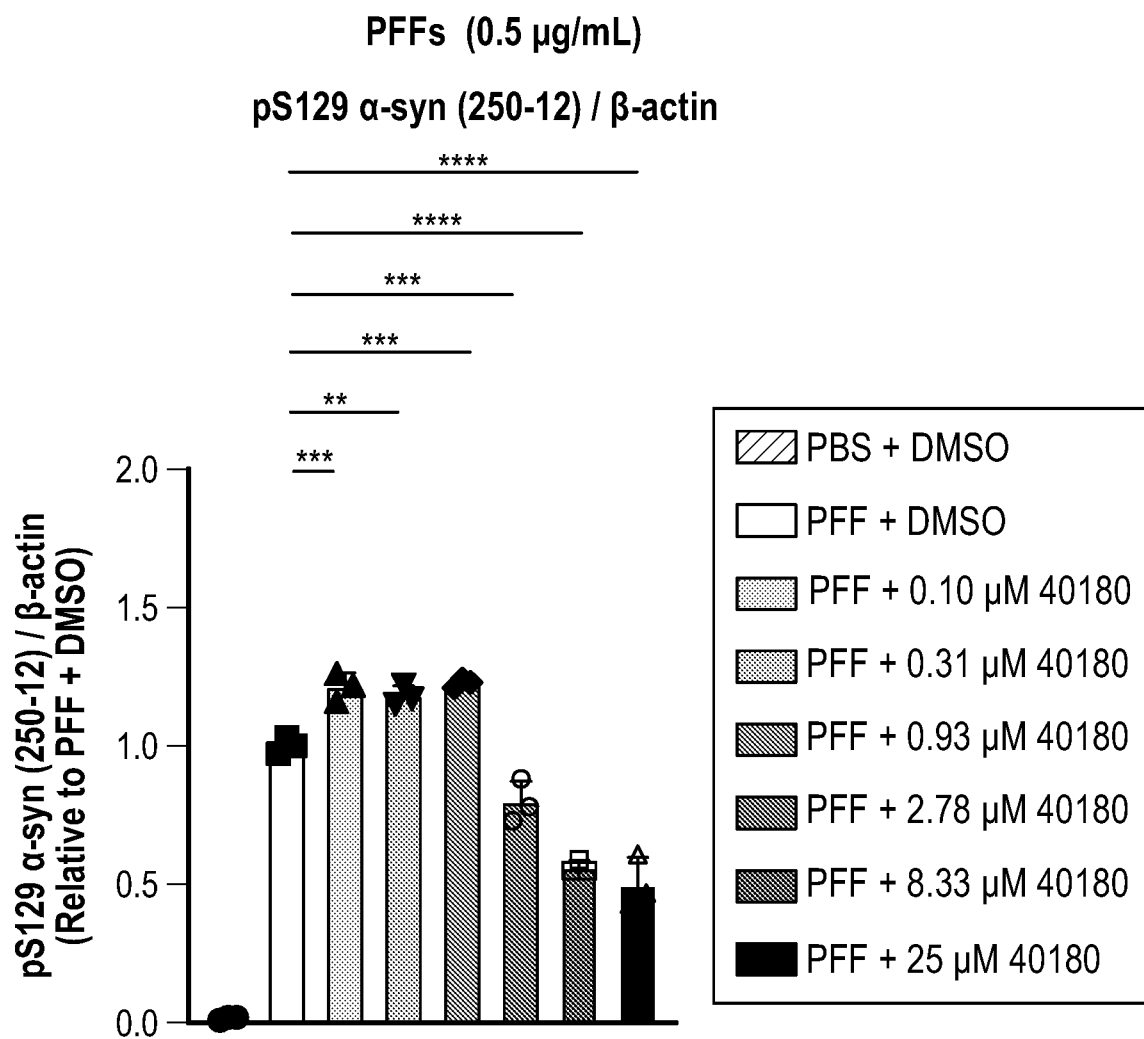


FIG. 17B

49/80

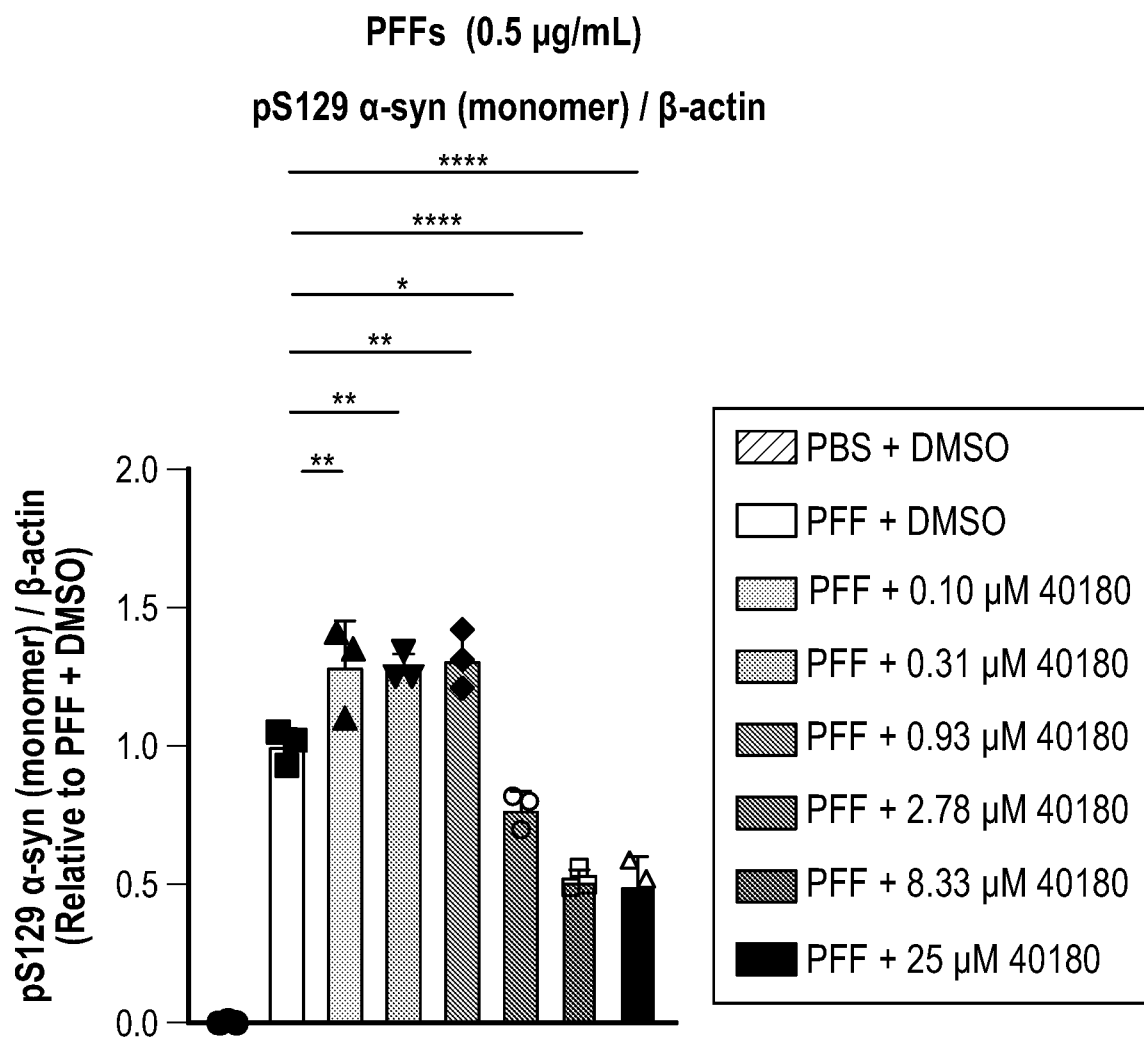


FIG. 17C

50/80

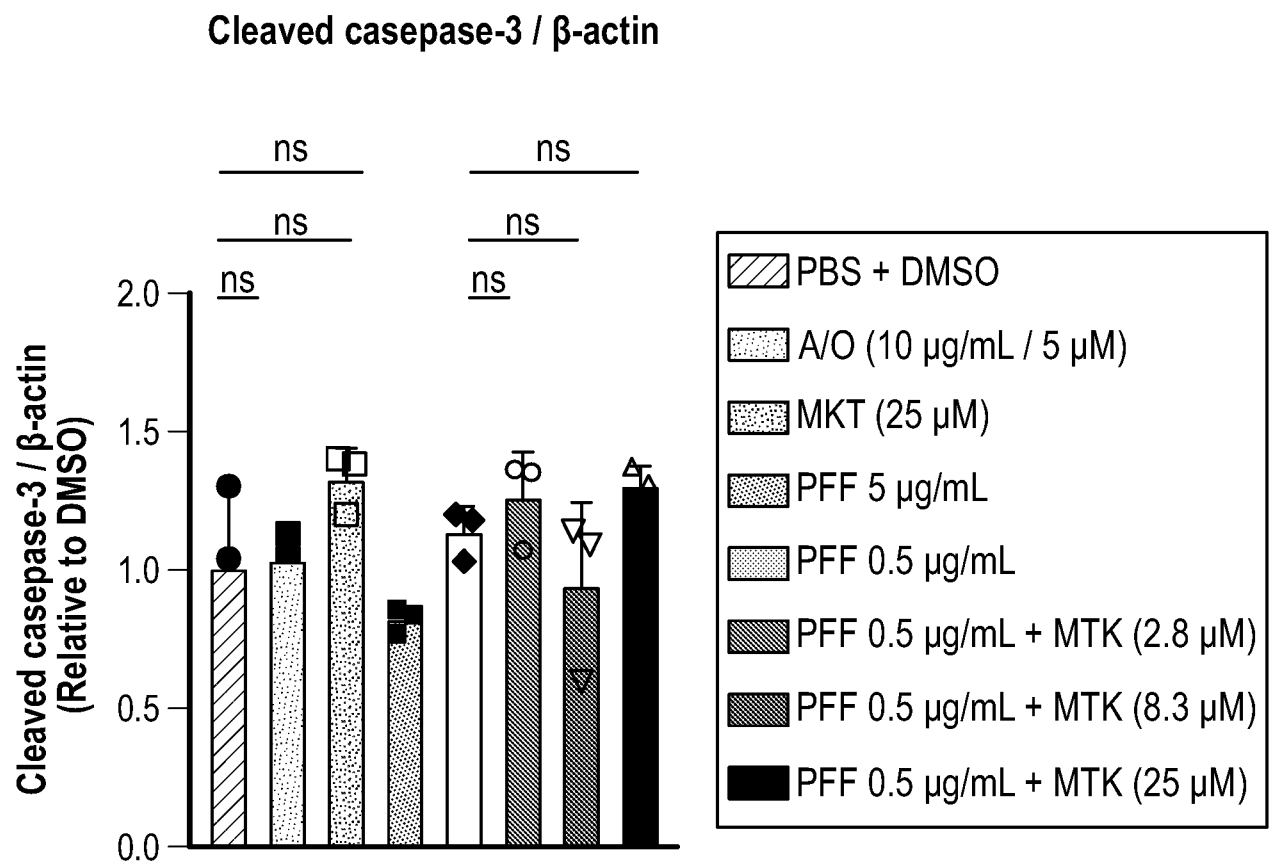


FIG. 18

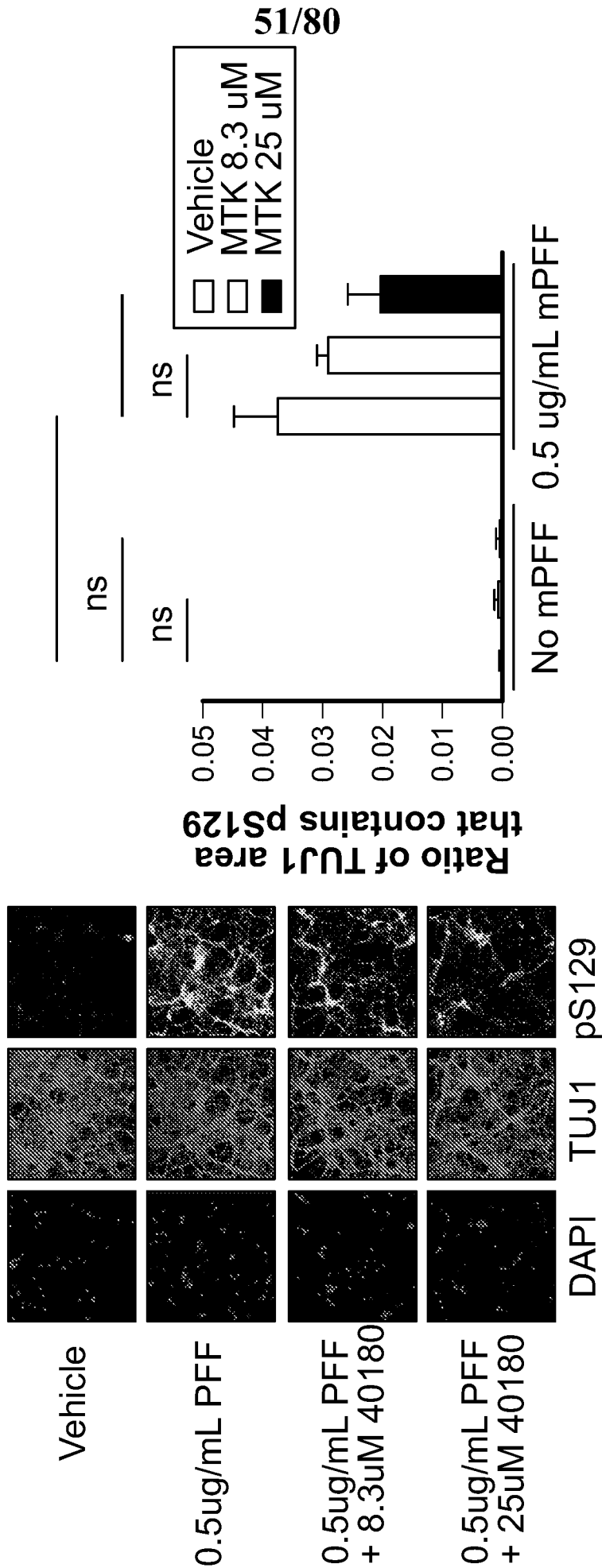


FIG. 19A

FIG. 19B

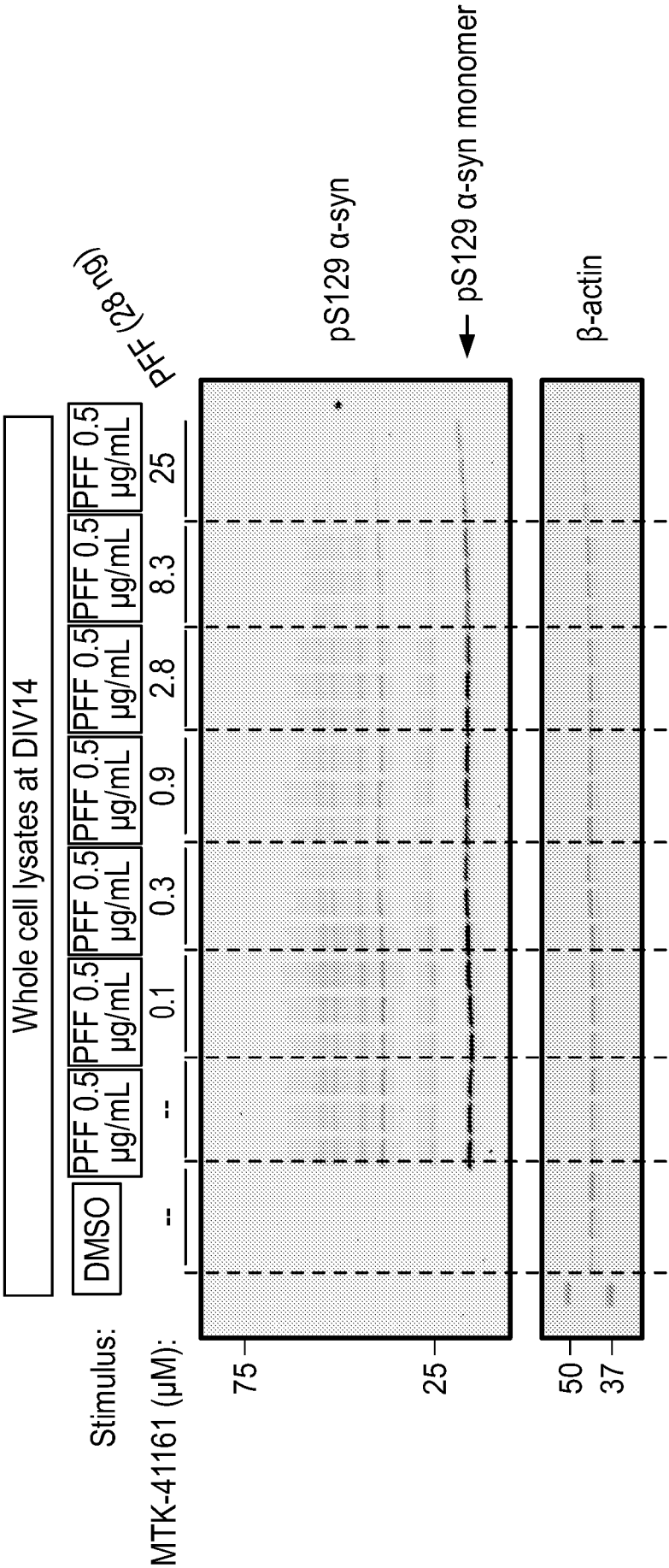


FIG. 20A

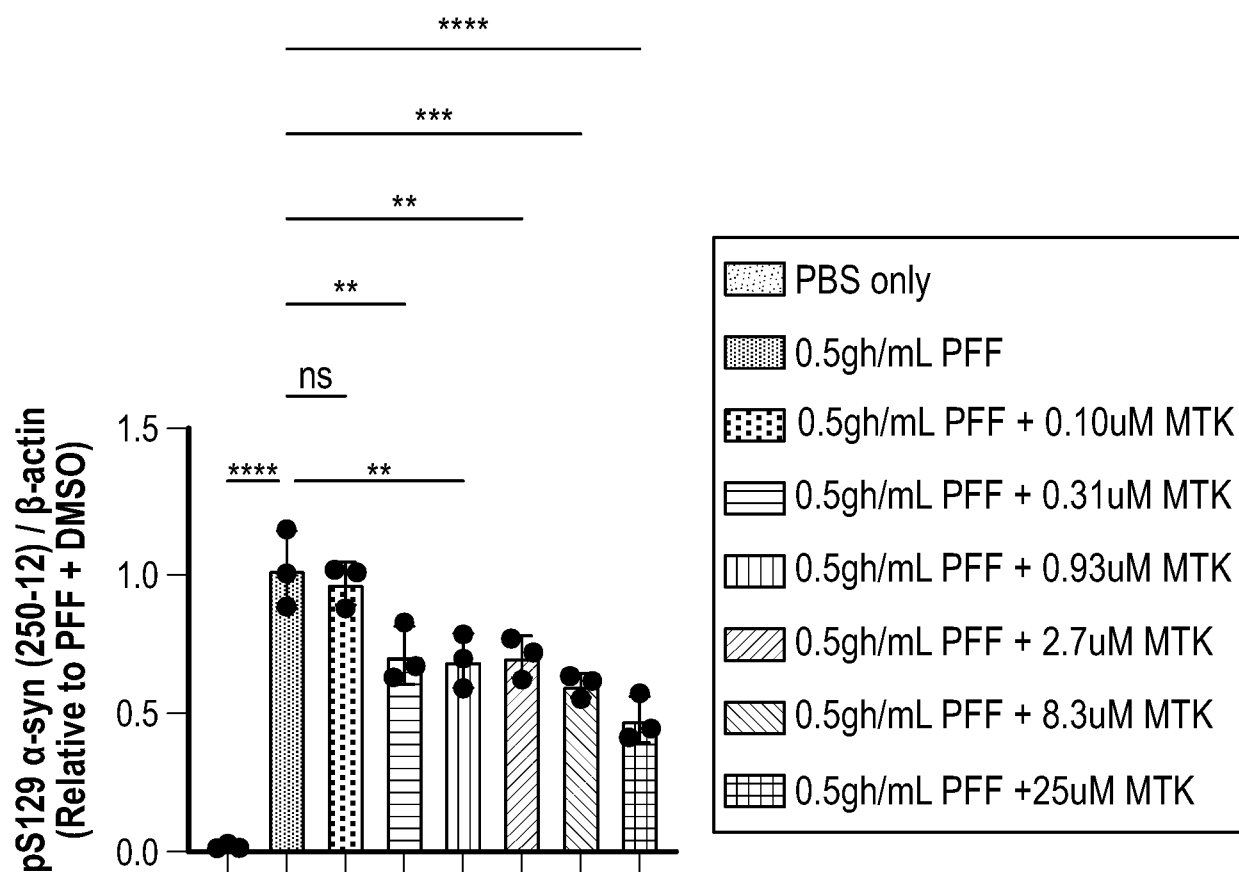


FIG. 20B

54/80

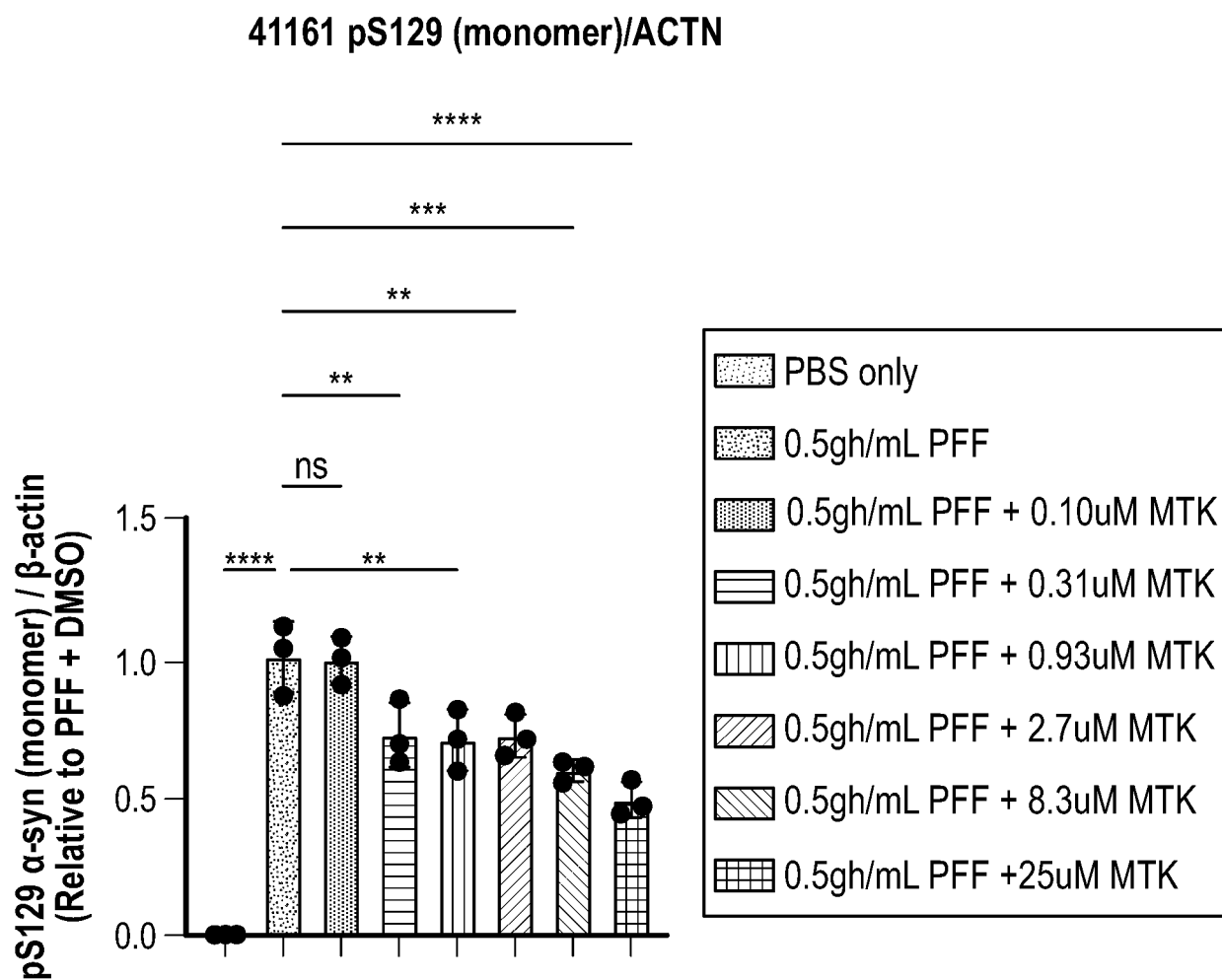


FIG. 20C

55/80

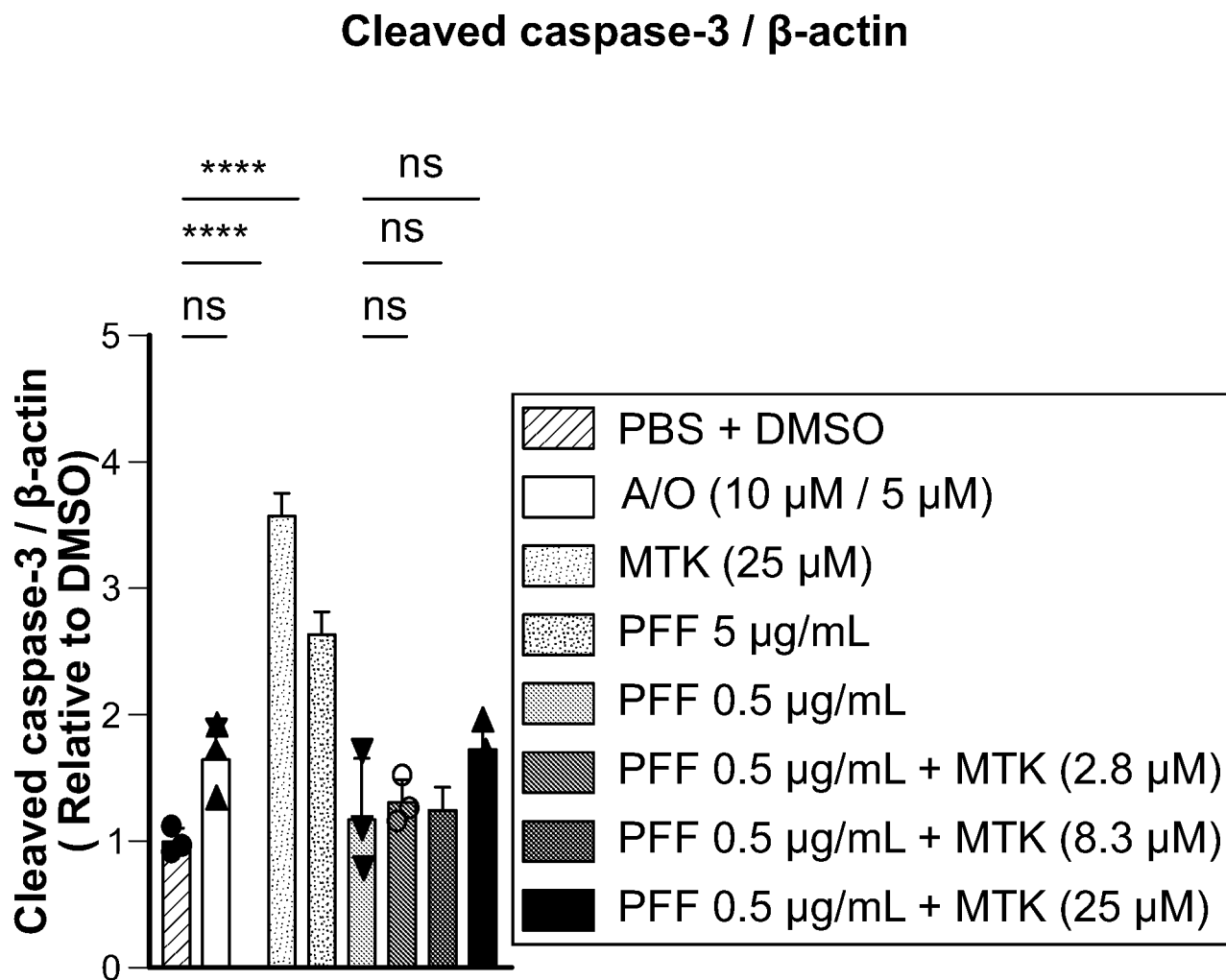


FIG. 21

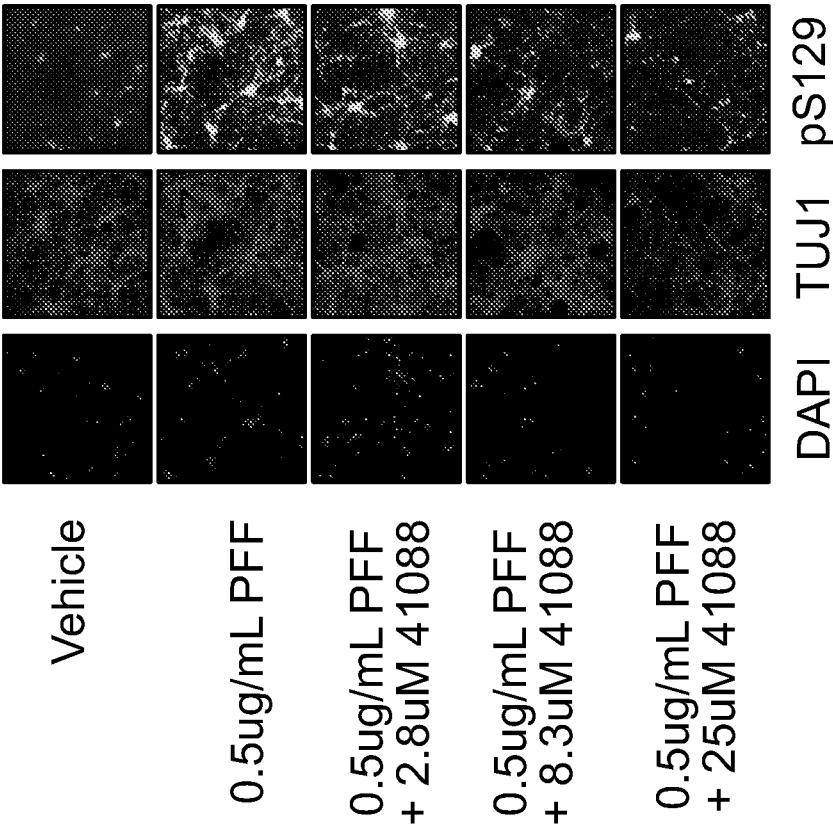


FIG. 22A

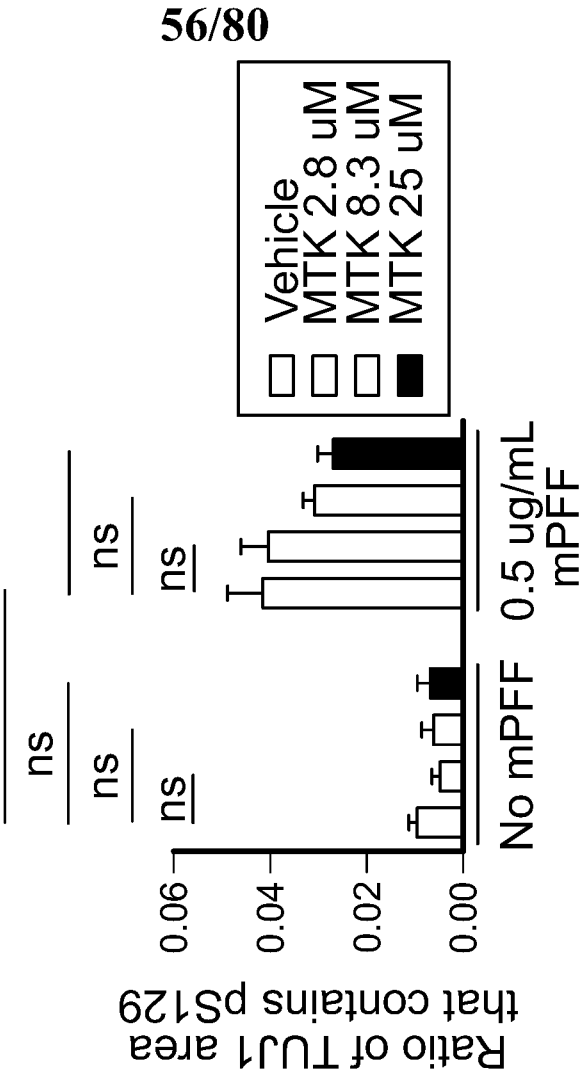


FIG. 22B

58/80

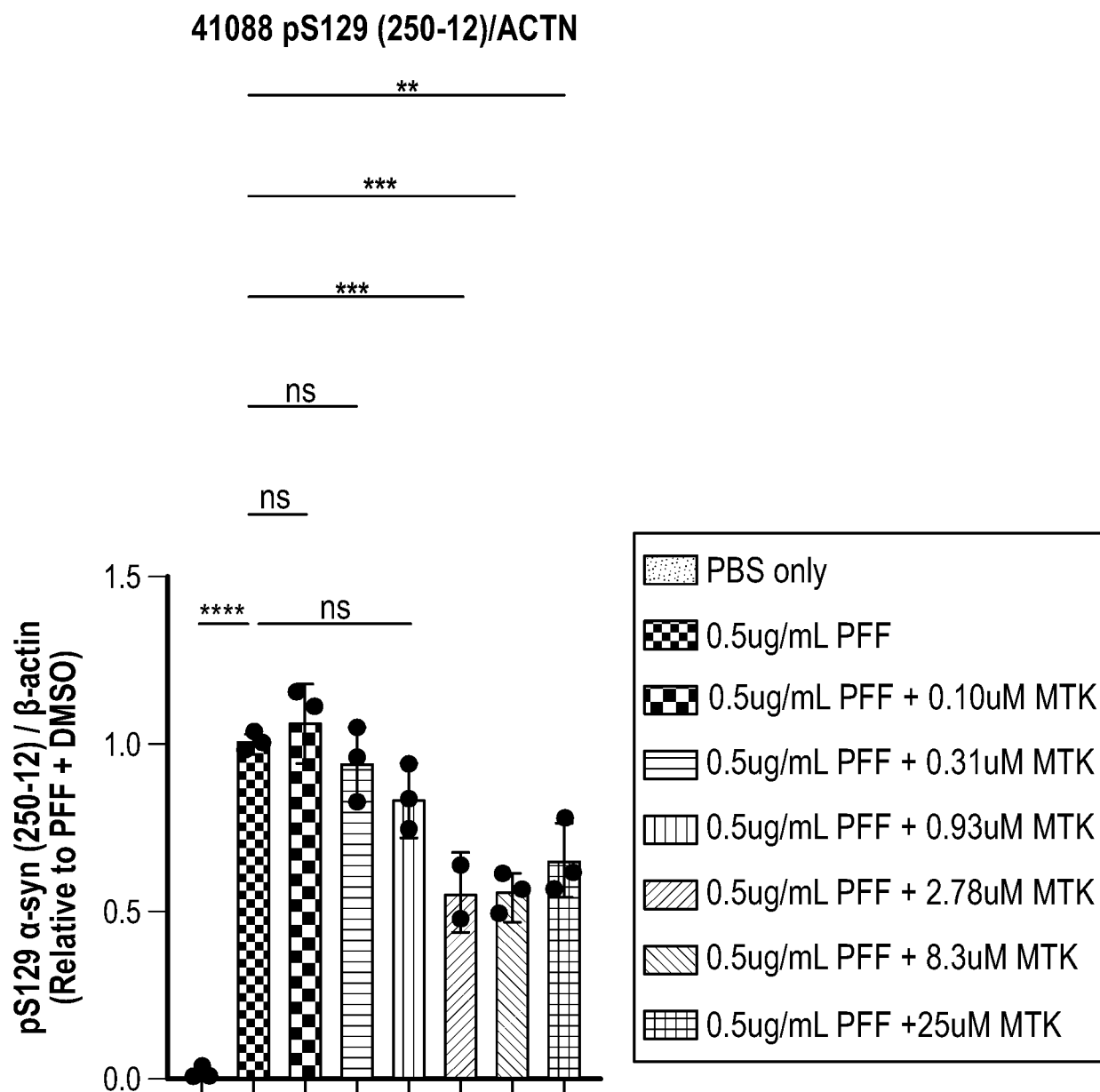


FIG. 23B

59/80

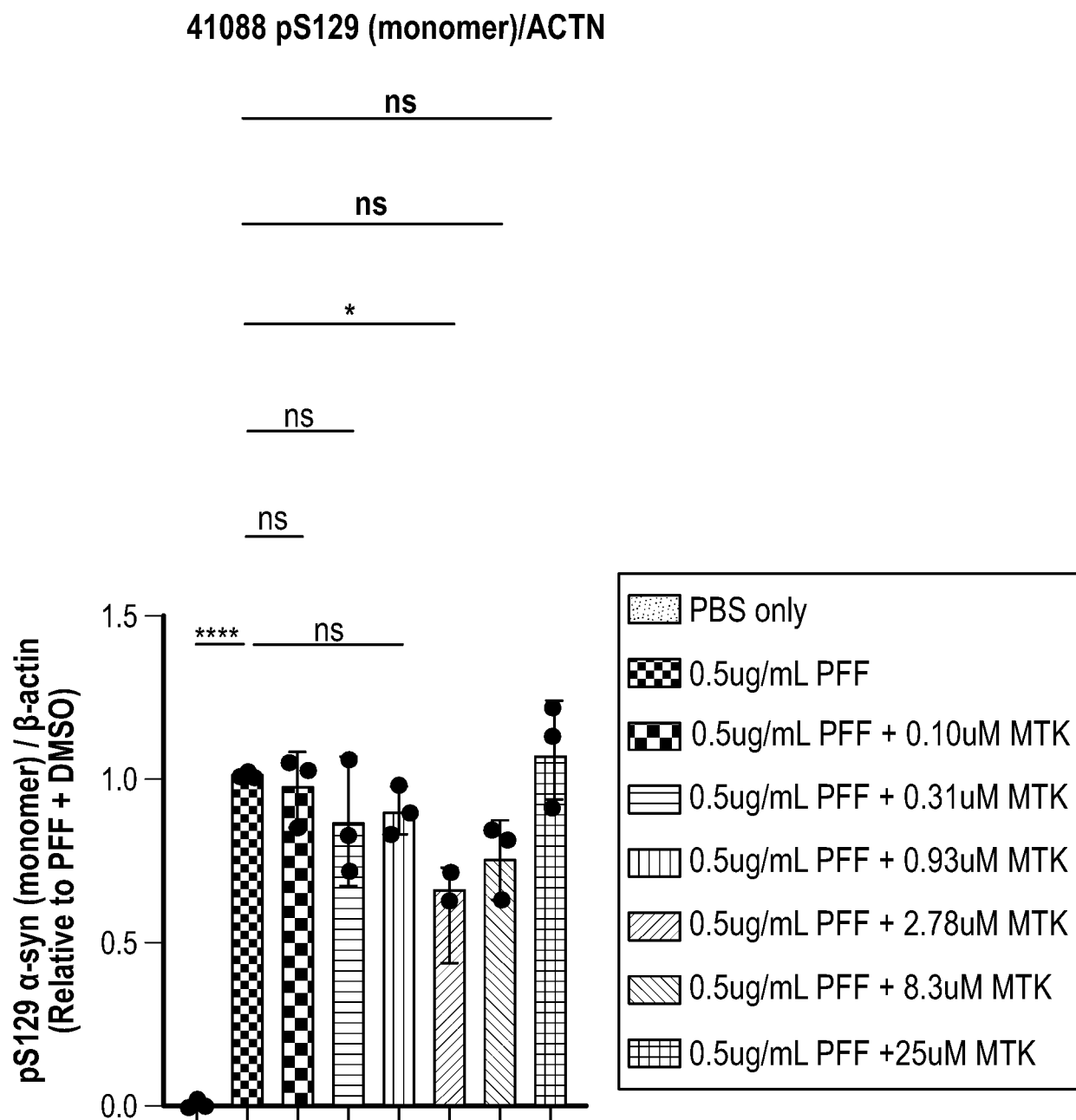


FIG. 23C

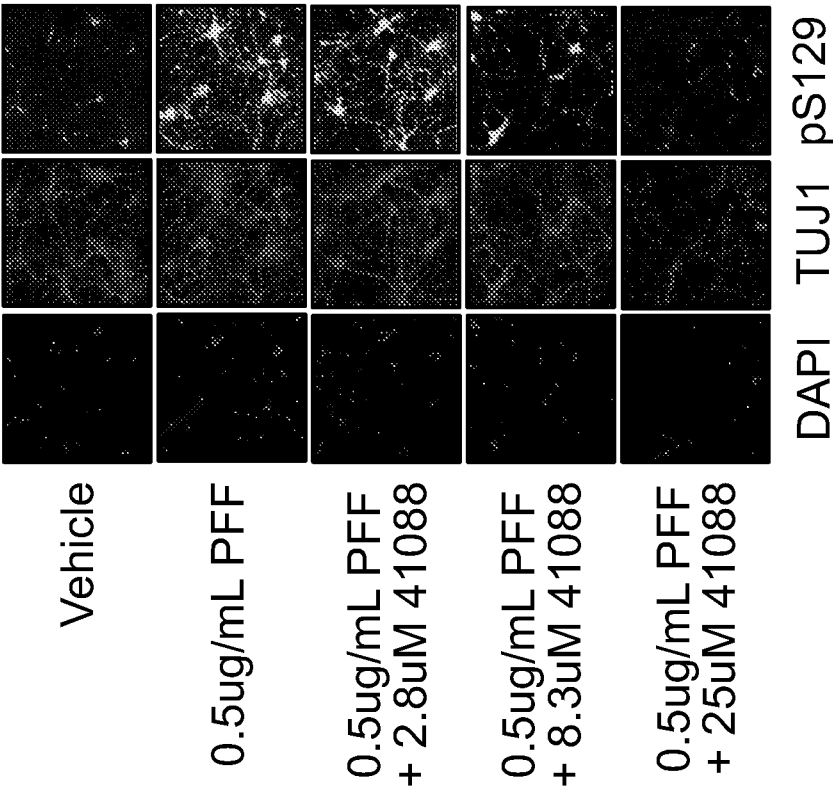


FIG. 24A

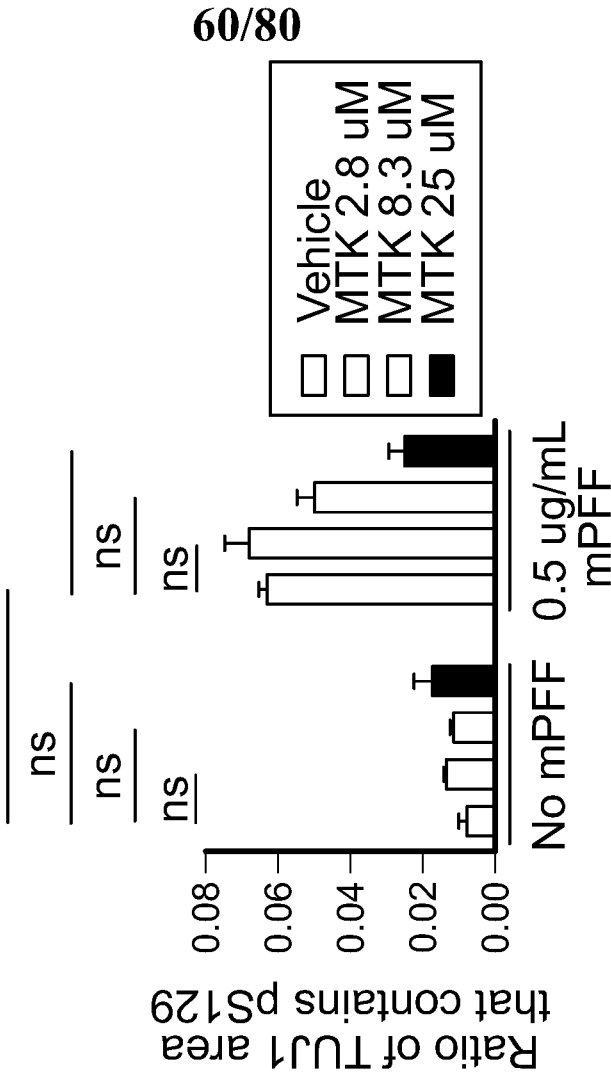
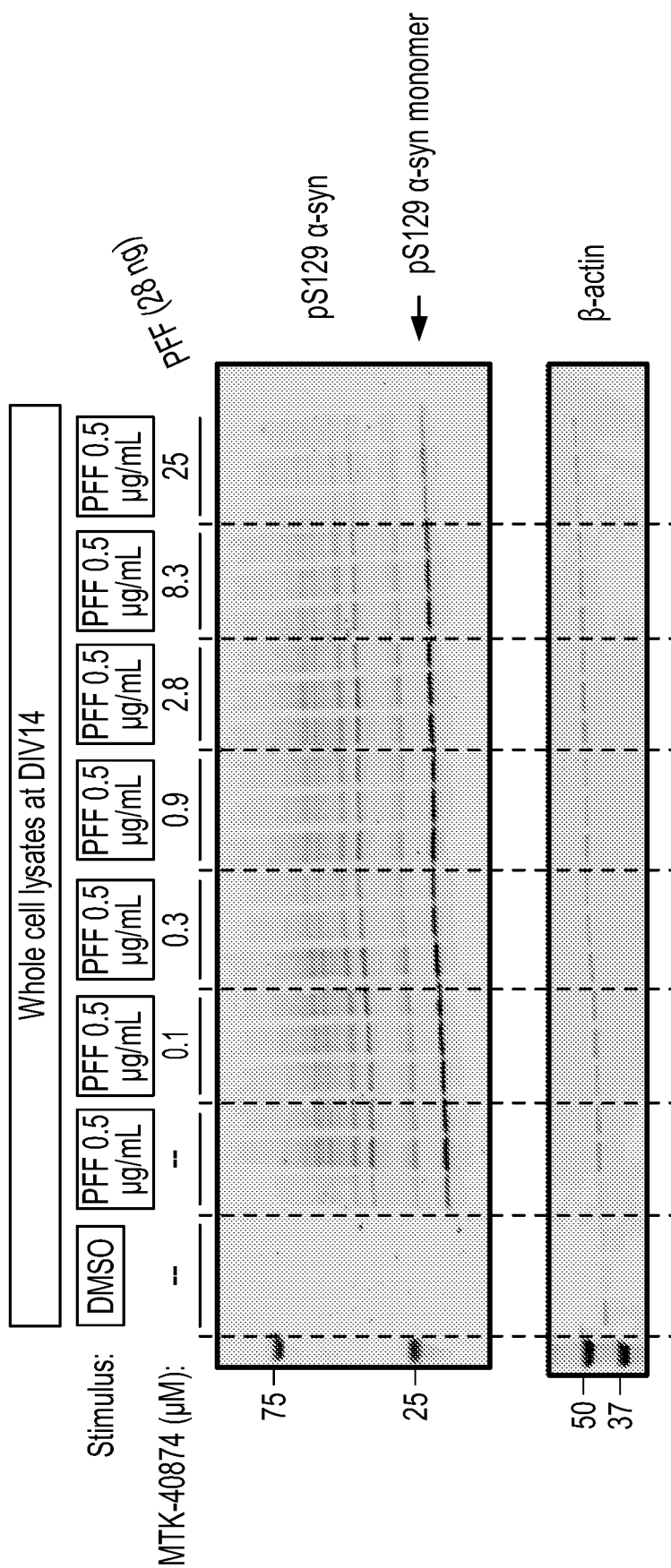


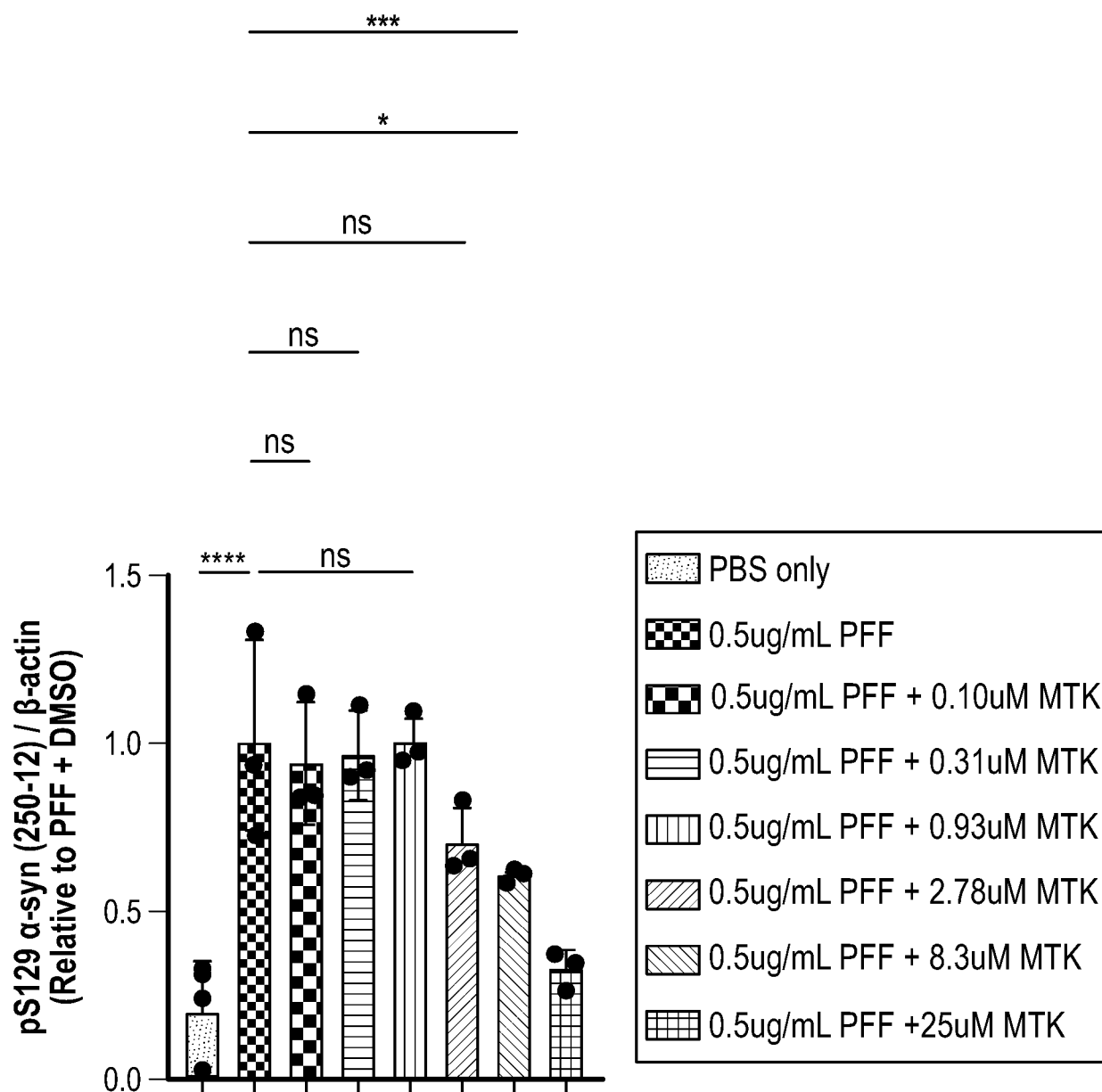
FIG. 24B

61/80



62/80

40874 pS129 (250-12)/ACTN



63/80

40874 pS129 (monomer)/ACTN

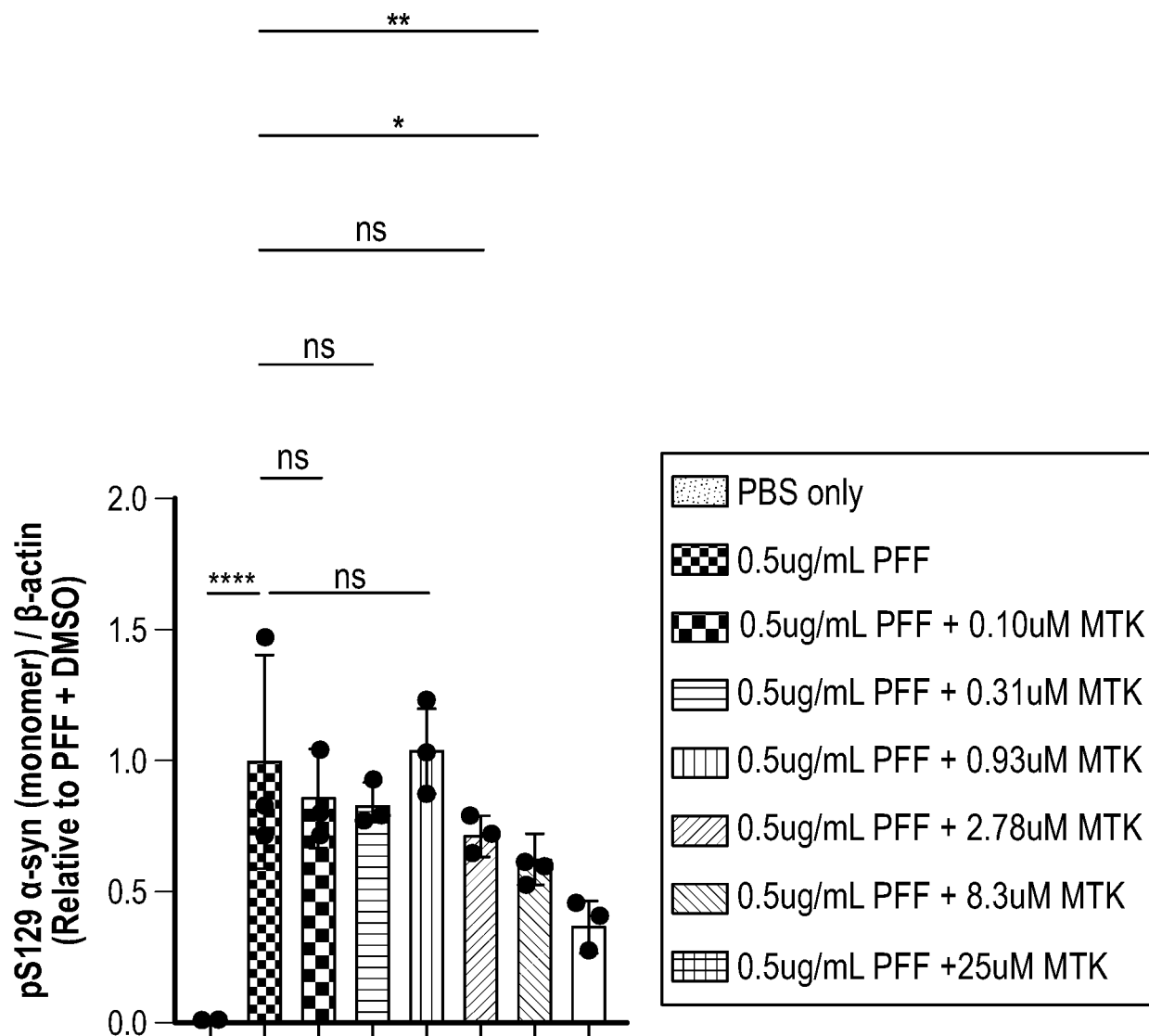
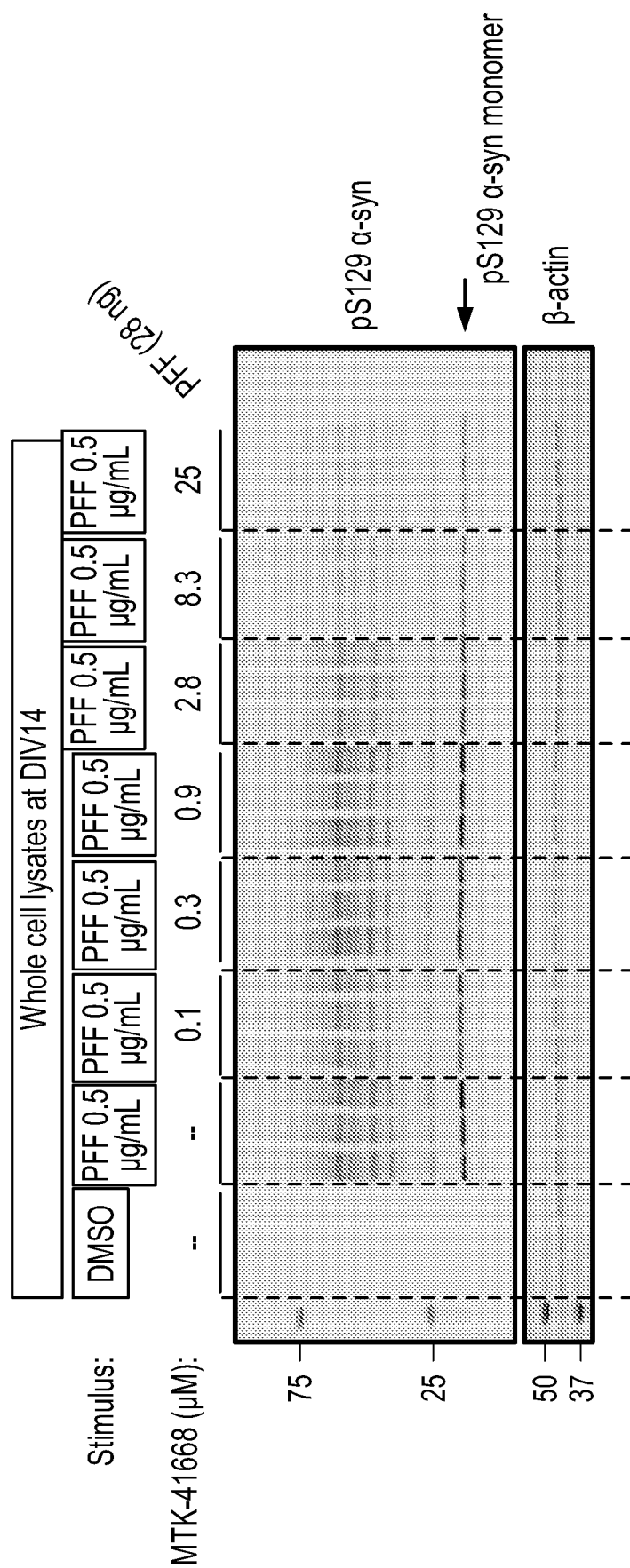


FIG. 25C



65/80

41668 pS129 (250-12)/ACTN

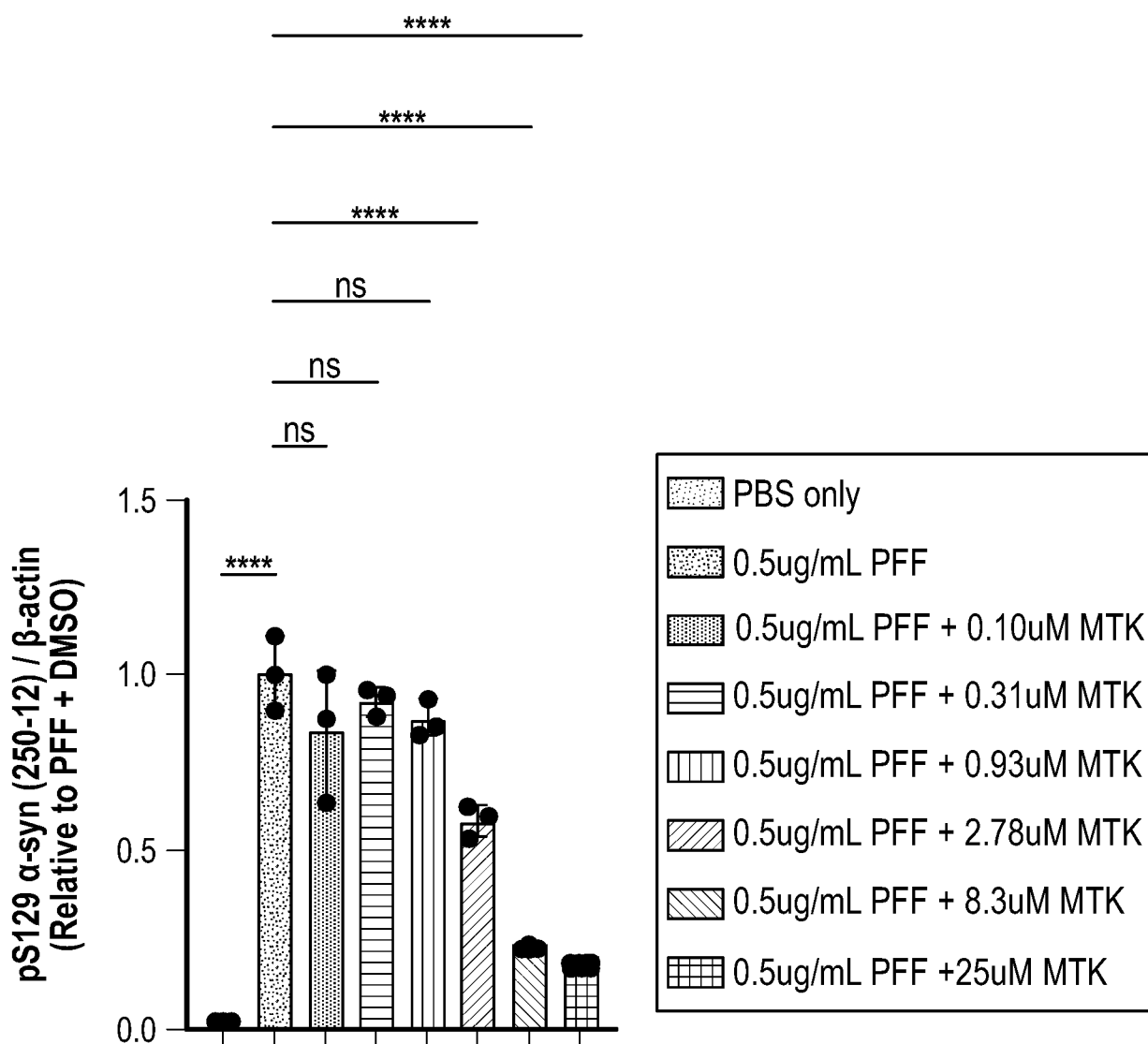


FIG. 26B

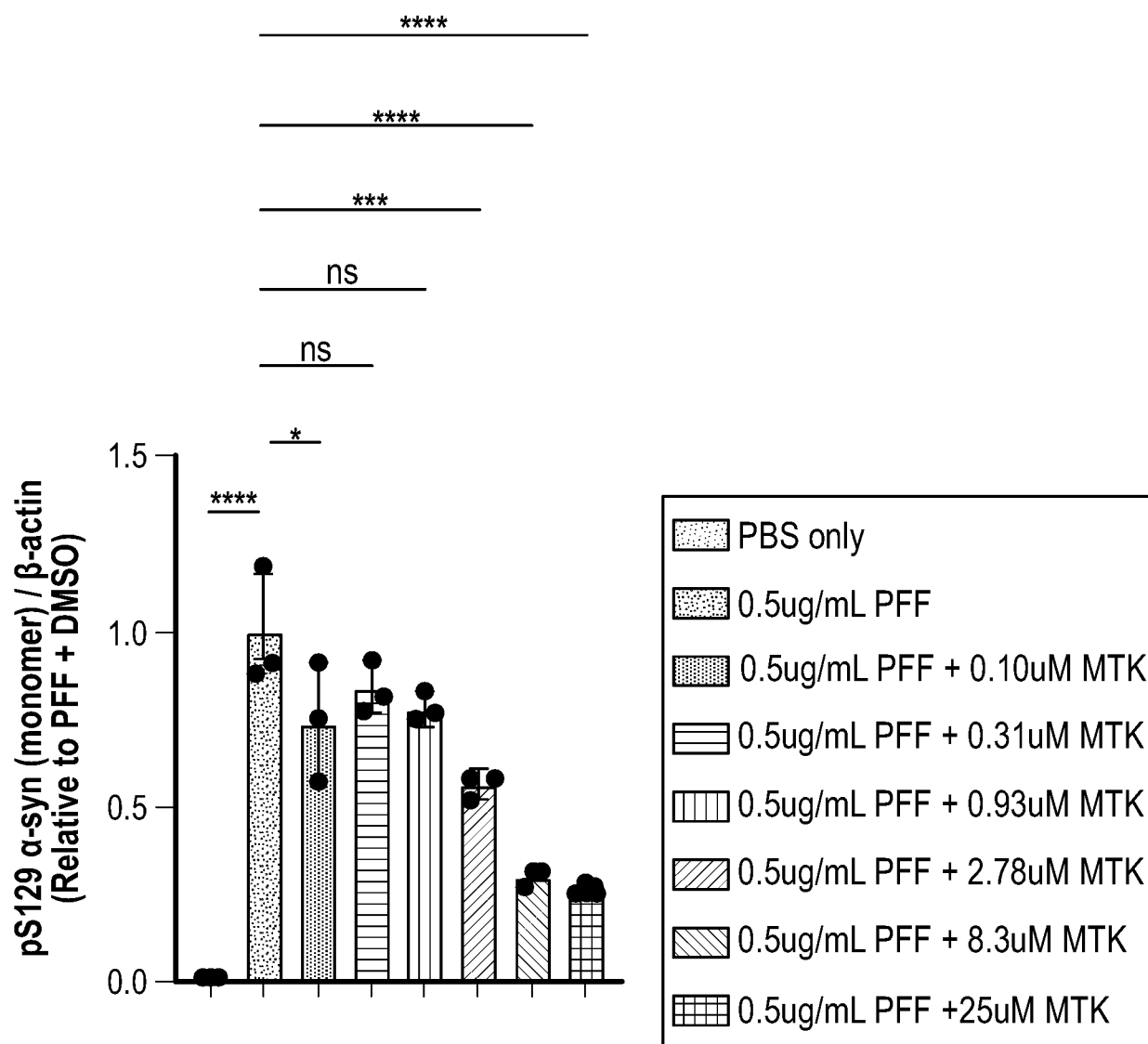
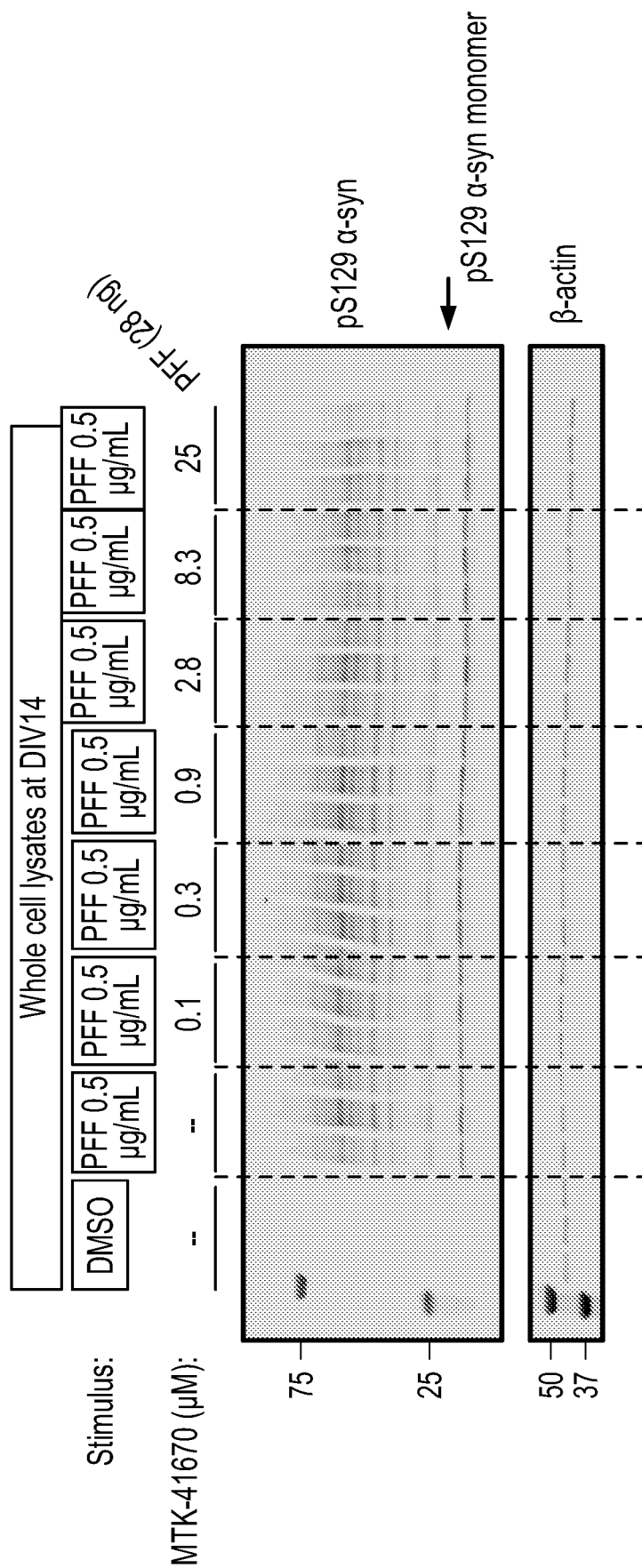


FIG. 26C



41670 pS129 (250-12)/ACTN

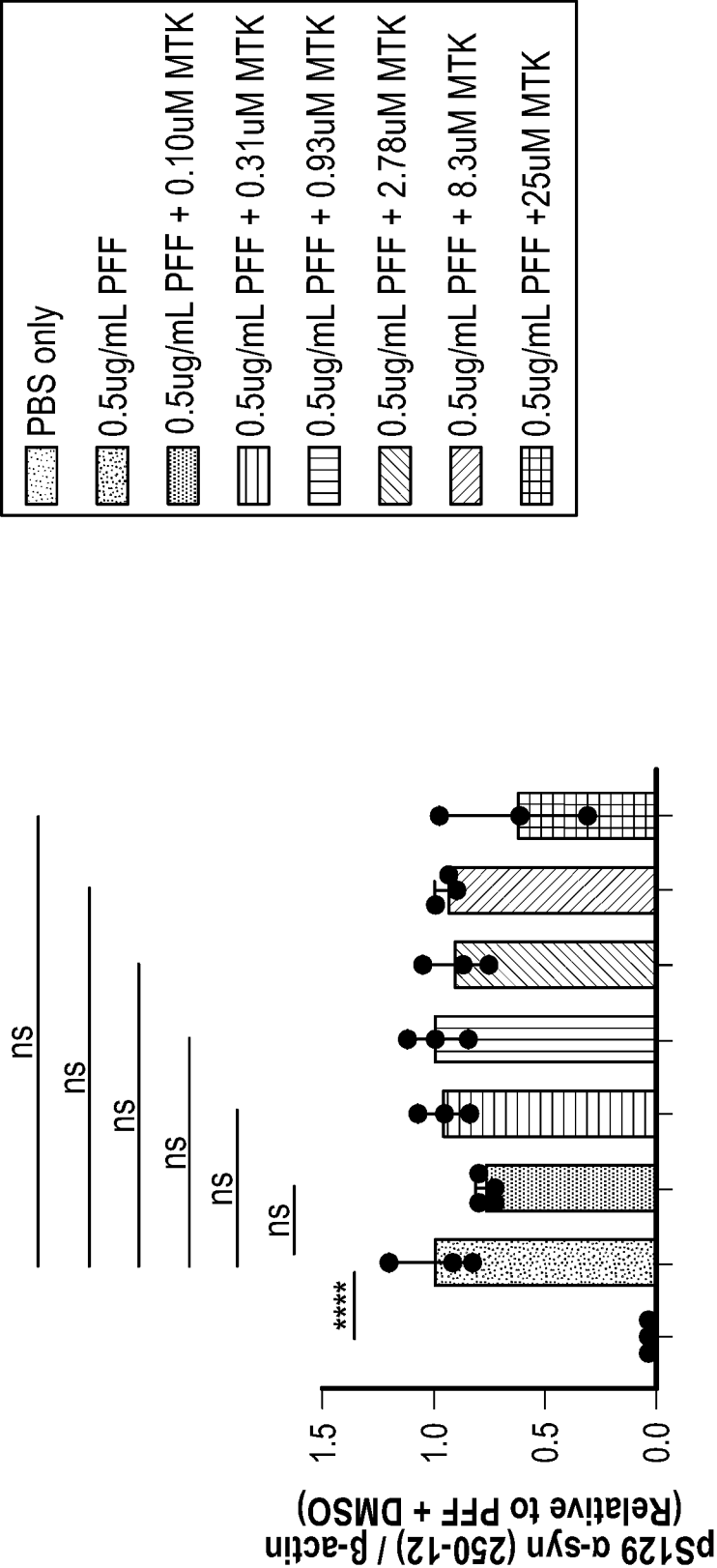


FIG. 27B

69/80

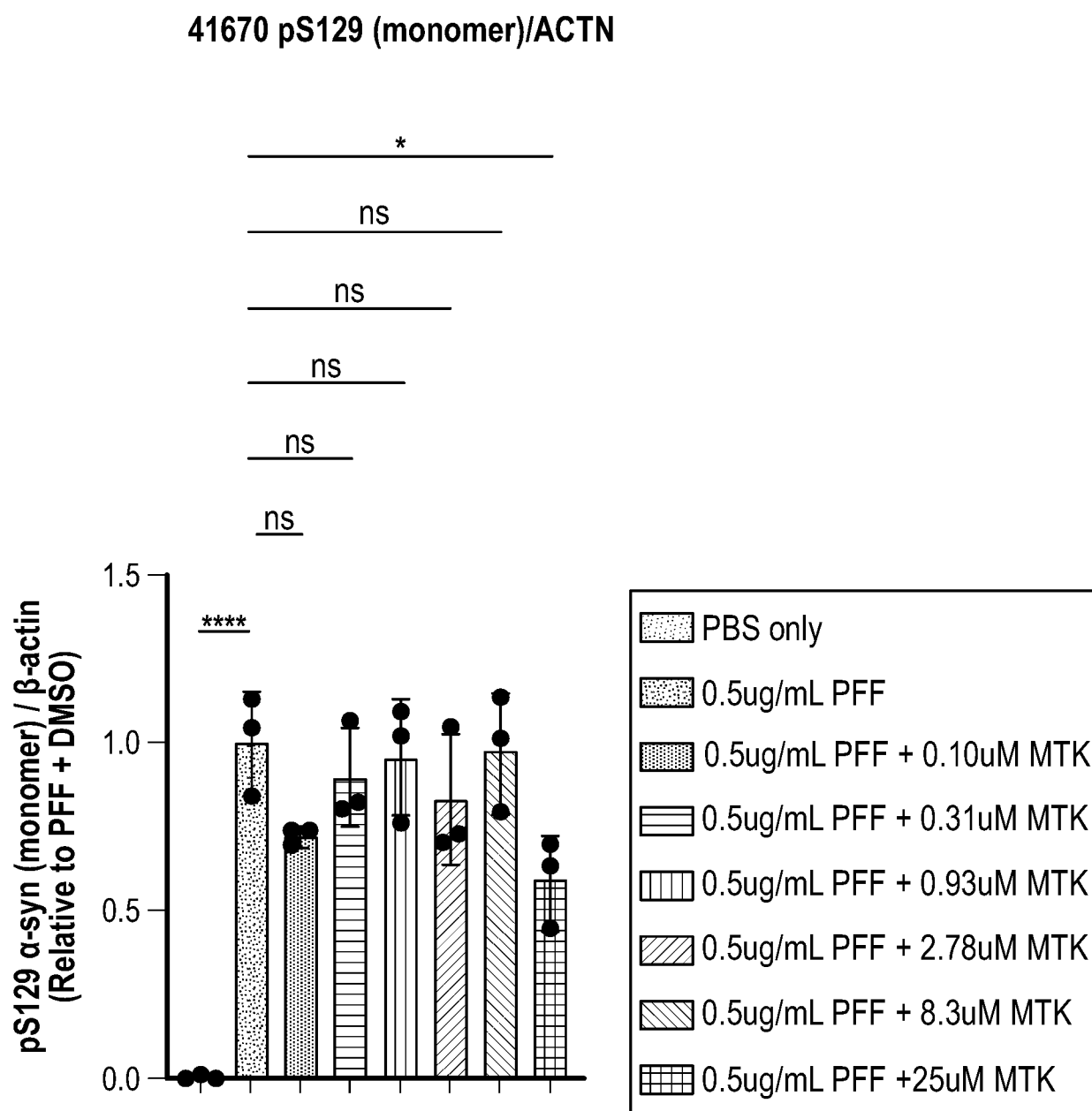
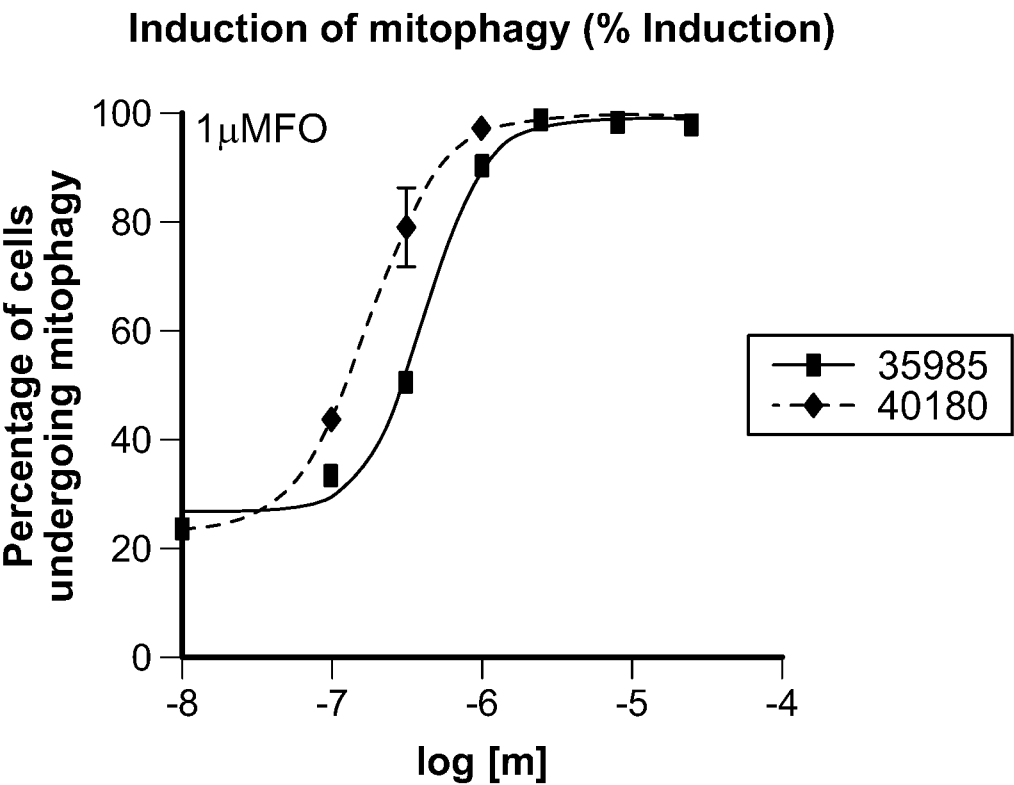


FIG. 27C

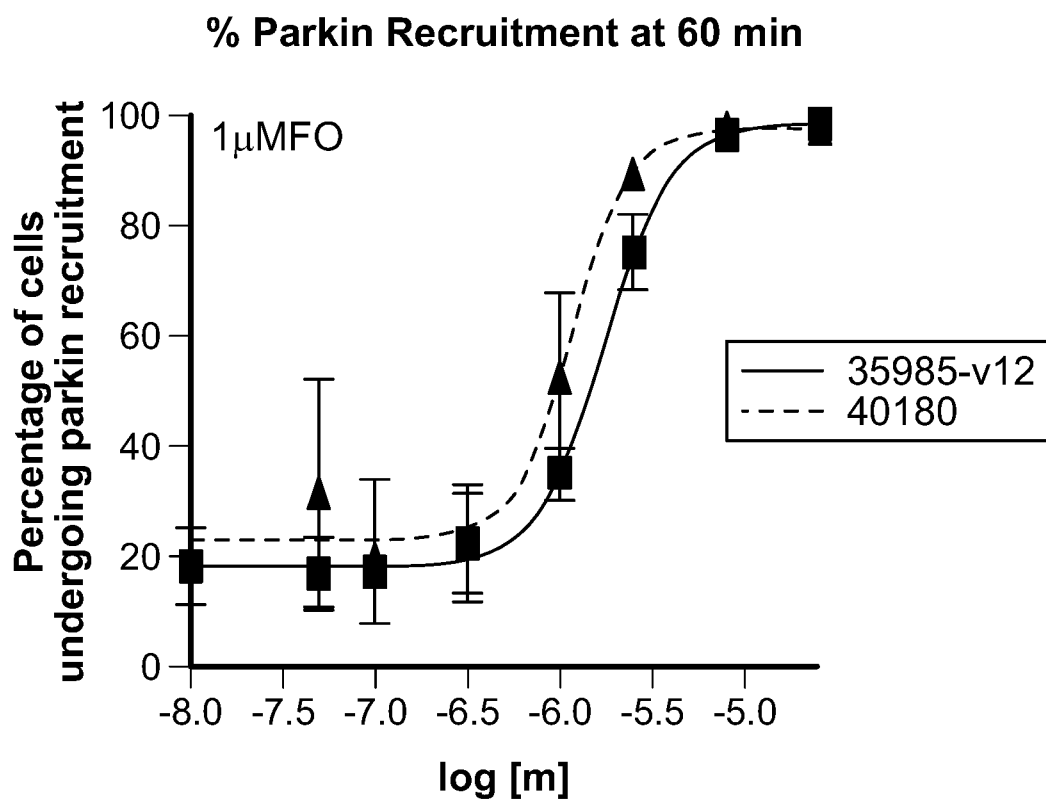
70/80



	35985	40180
EC50	3.718e-007 to 4.782e-007	1.536e-007 to 2.049e-007

FIG. 28

71/80



		35985-v12	40180
EC50		1.744e-006	1.15e-006

FIG. 29

Cisplatin causes mitochondrial damage in vivo:
pS65-Ub increase

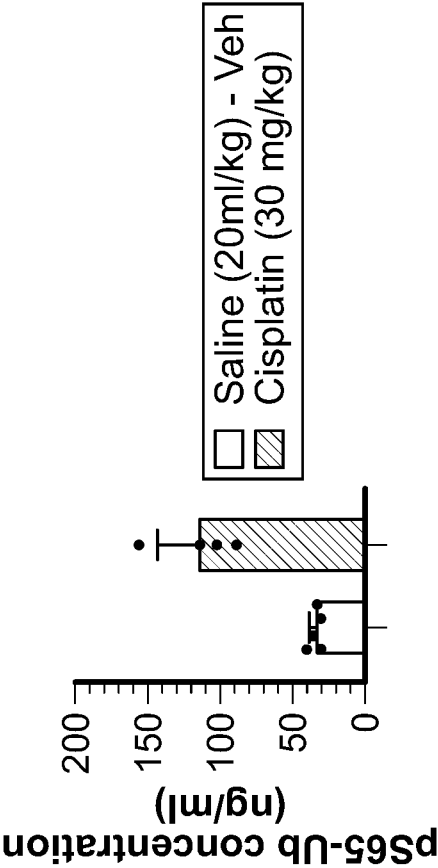


FIG. 30A

Cisplatin causes mitochondrial damage in vivo:
Induction of PINK1

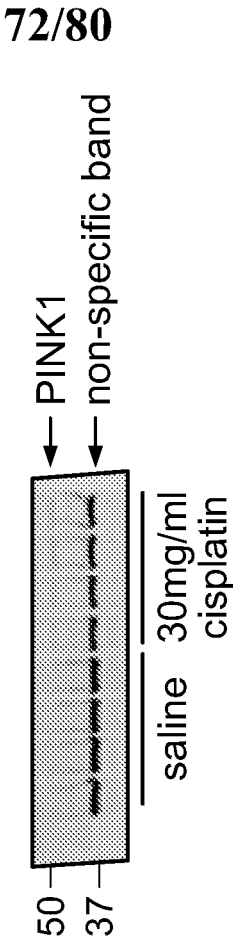


FIG. 30B

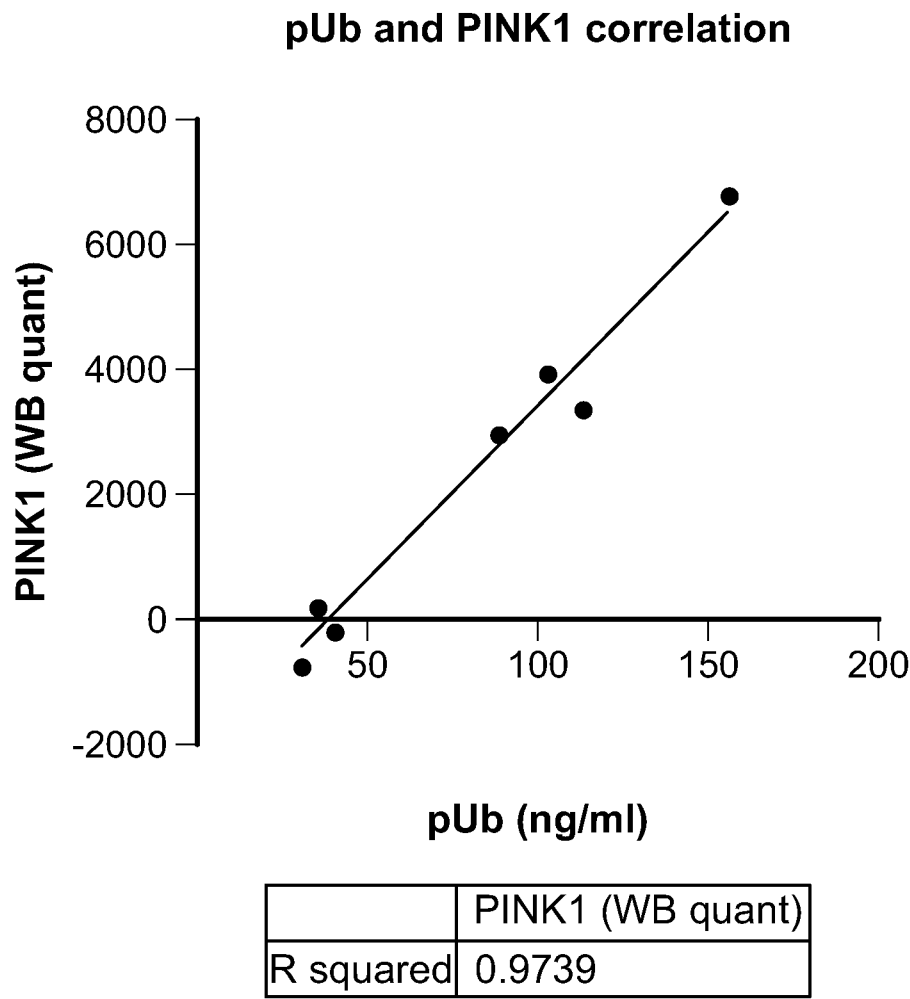


FIG. 30C

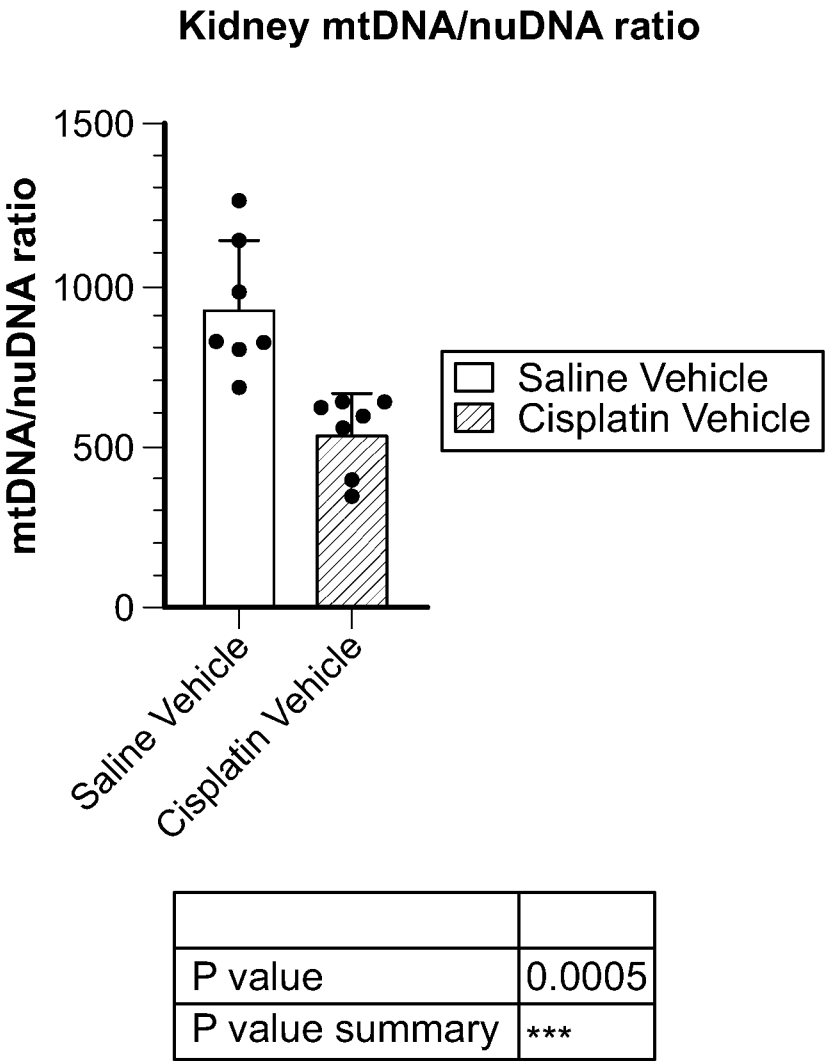


FIG. 31

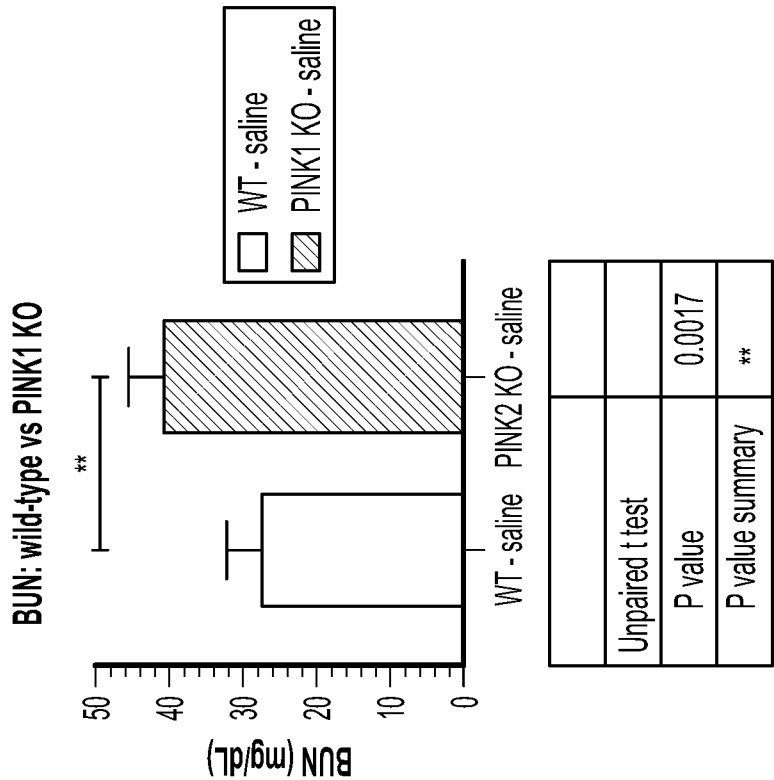


FIG. 32A

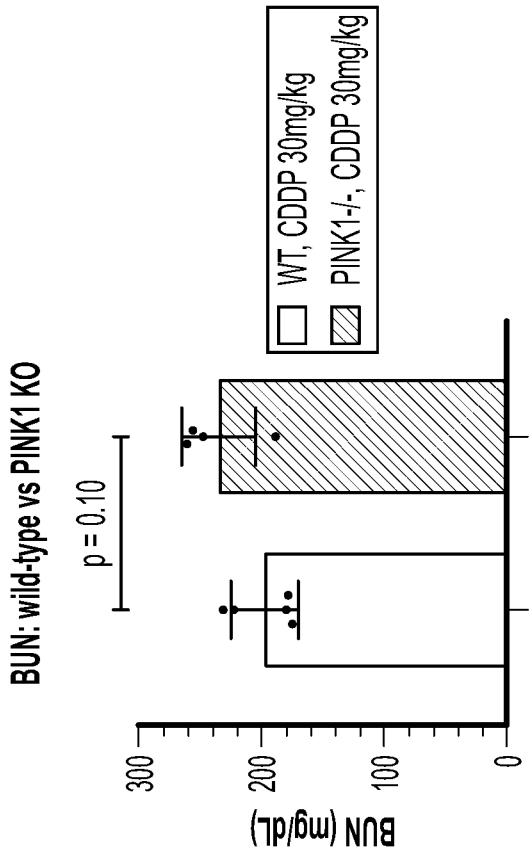
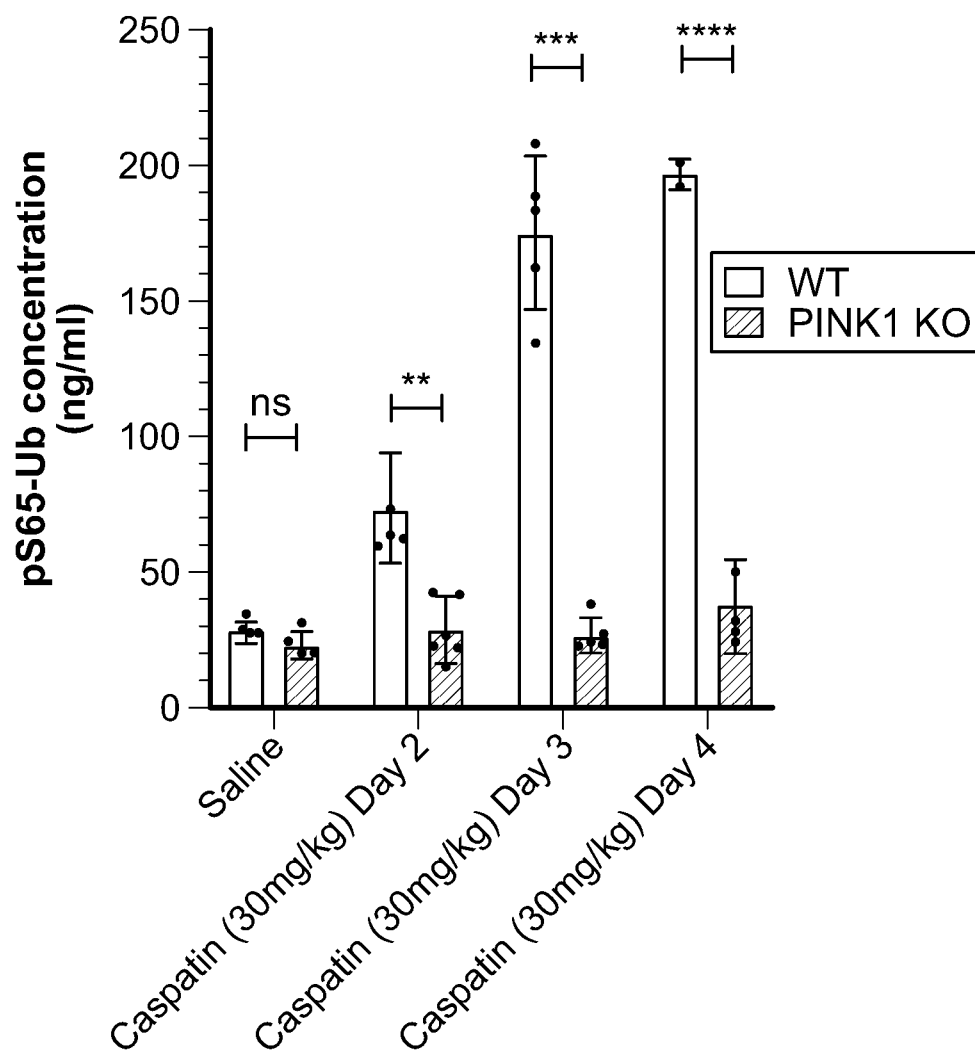
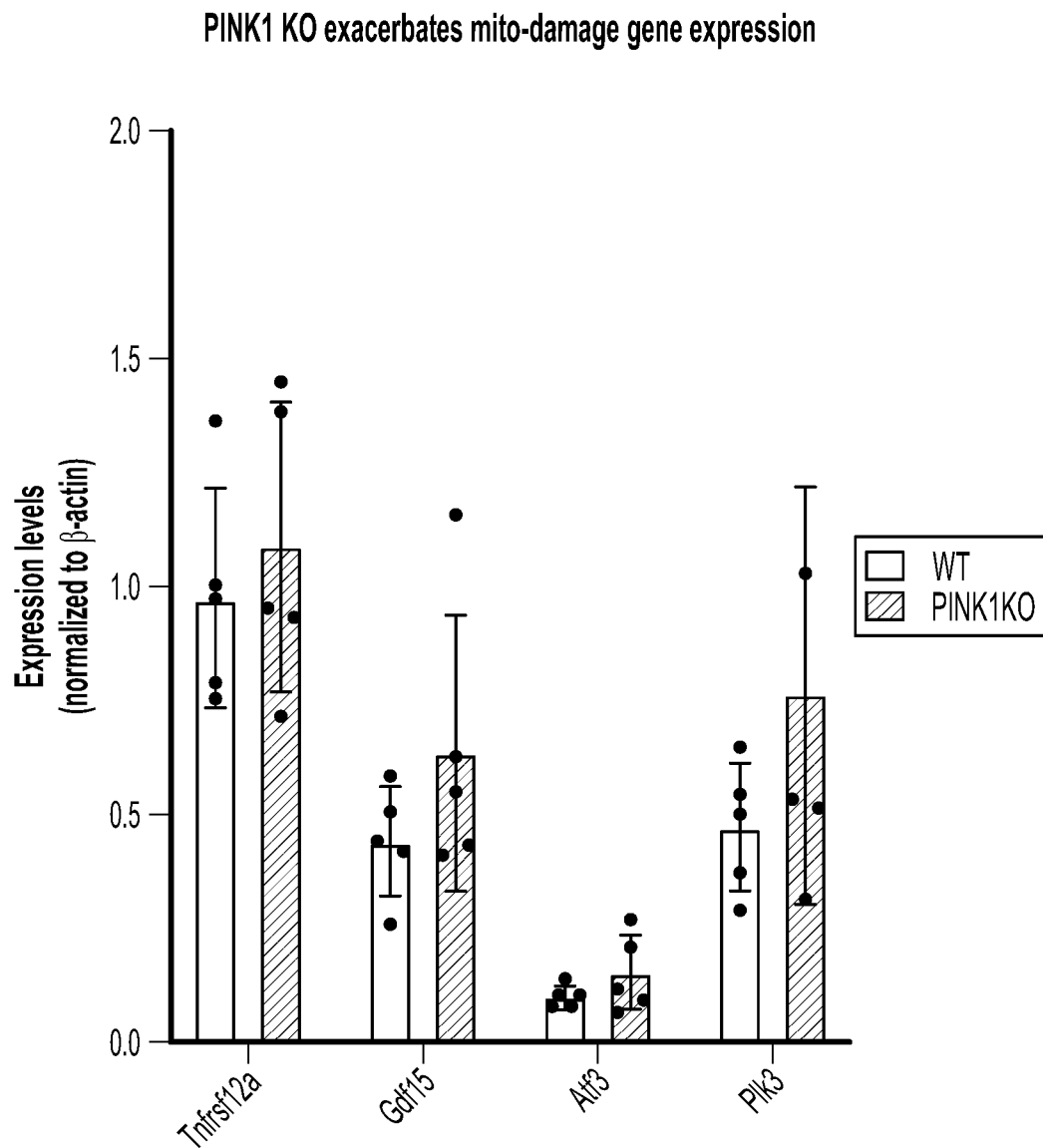


FIG. 32B

76/80

PINK1 pathway engagement eliminated in PINK1 KO mouse**FIG. 33**

77/80



Source of Variation	% of total variation	P Value	P value summary	Significant?
Interaction	1.246	0.7336	ns	No
Genes	63.76	<0.0001	****	Yes
Genotype	4.024	0.0498	*	Yes

FIG. 34

	Cmax (uM, mean)	
dosage group (PO, mg/kg)	40180 single dose	MTK458 single dose
10	0.35	0.49
25	1.15	
50	9.21	6.98
100	19.43	

	AUClast (hr*uM, mean)	
dosage group (PO, mg/kg)	40180 single dose	MTK458 single dose
10	0.51	1.79
25	1.91	
50	17.27	30.50
100	85.57	

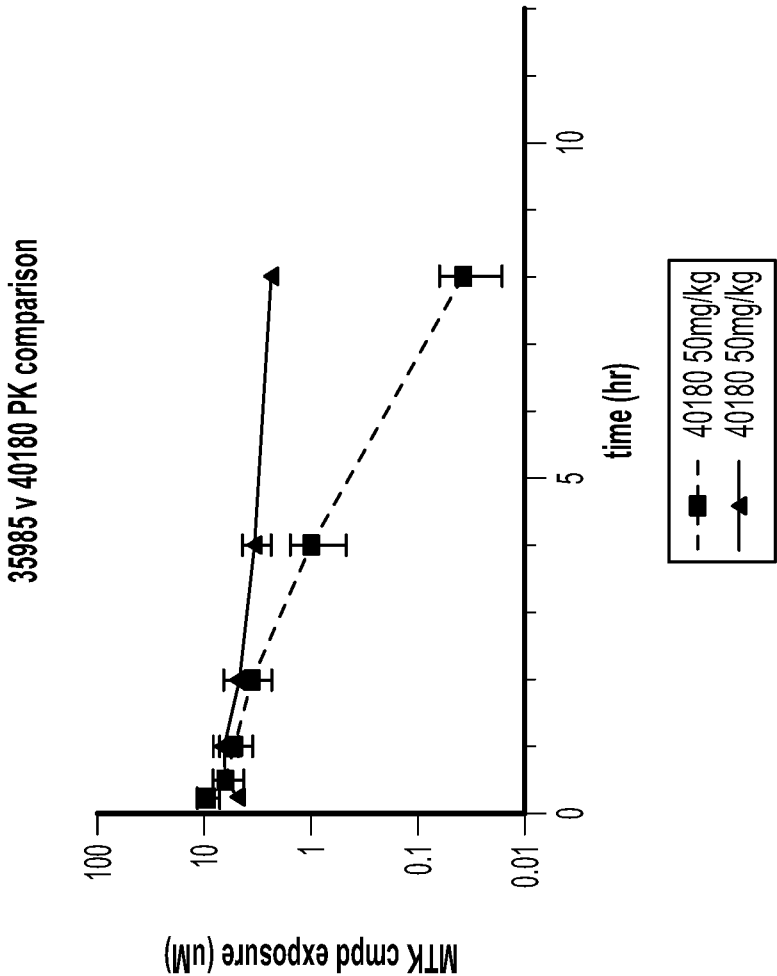


FIG. 35

79/80

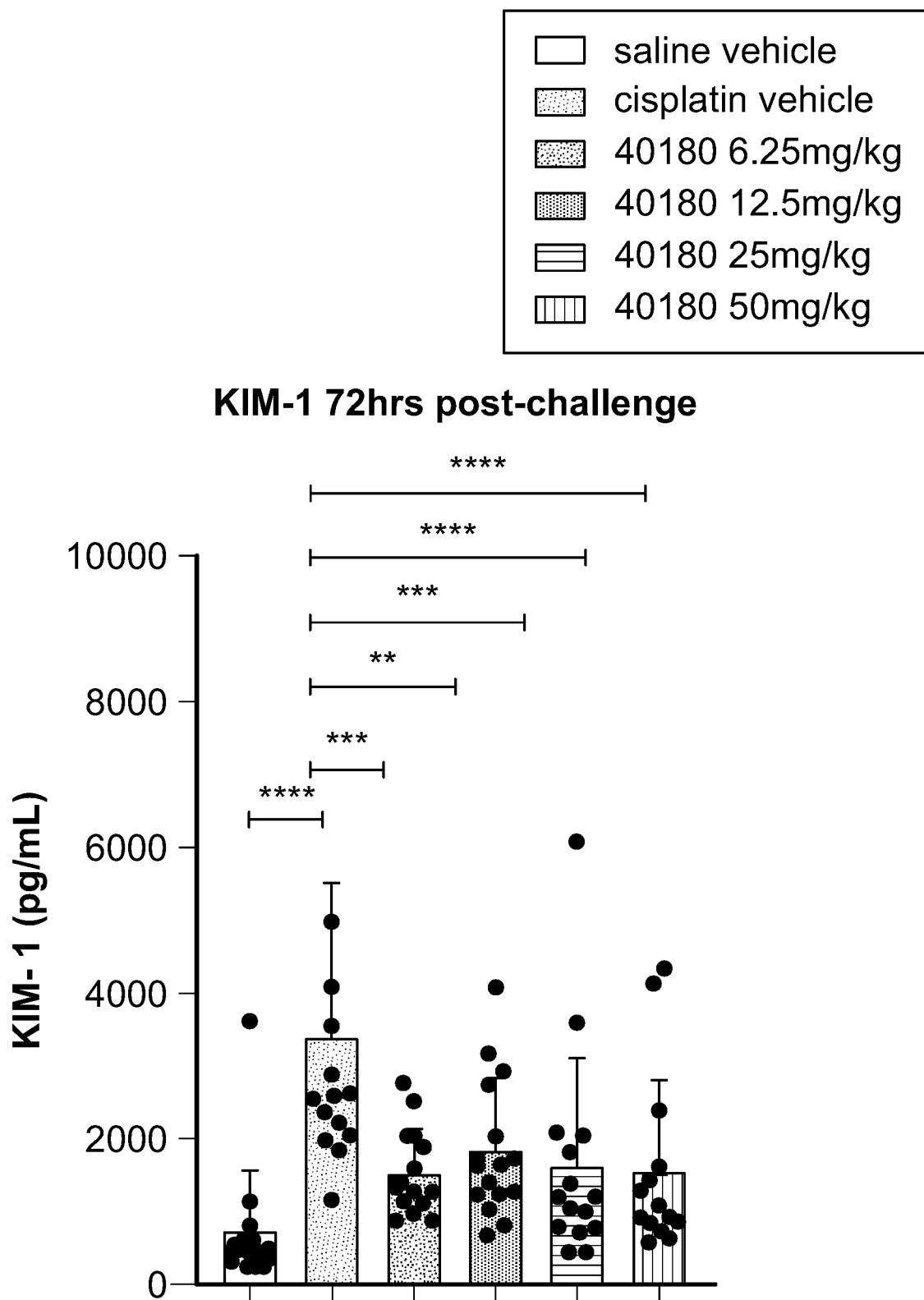


FIG. 36

80/80

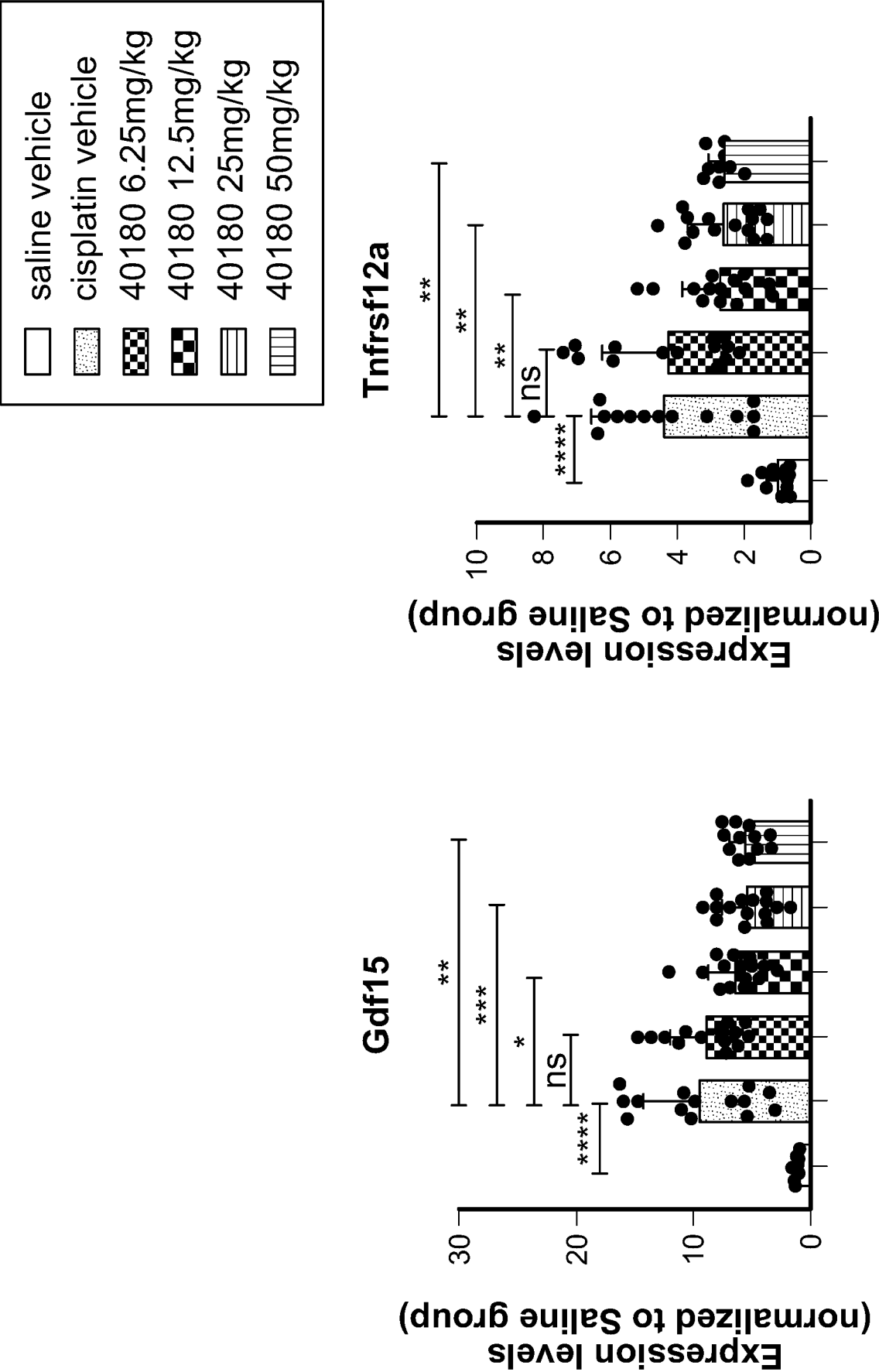


FIG. 37