Correctors of the major Cystic Fibrosis mutant interact through membrane spanning domains

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MOLECULAR PHARMACOLOGY

SUPPLEMENTAL DATA

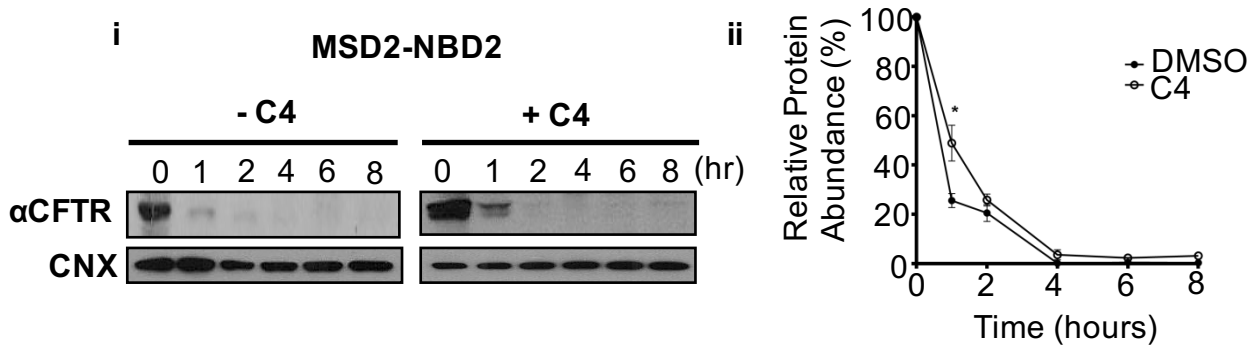

FIGURE S1: C4 stabilizes MSD2-NBD2 of CFTR. (**i**) MSD2-NBD2 domains of CFTR were expressed in HEK293 cells in the presence or absence of C4 (10μM) at 27 °C. After 24 h, protein synthesis was inhibited by addition of cycloheximide (0.5 mg/mL) with or without C4 (10μM), and cells collected after the indicated times for Western blot analysis of whole cell extracts. (**Ii**) The amount of CFTR protein at each time point was quantitated and expressed relative to that at time 0 and calnexin loading. Data are representative of 3 biological studies (*$p<0.05$).

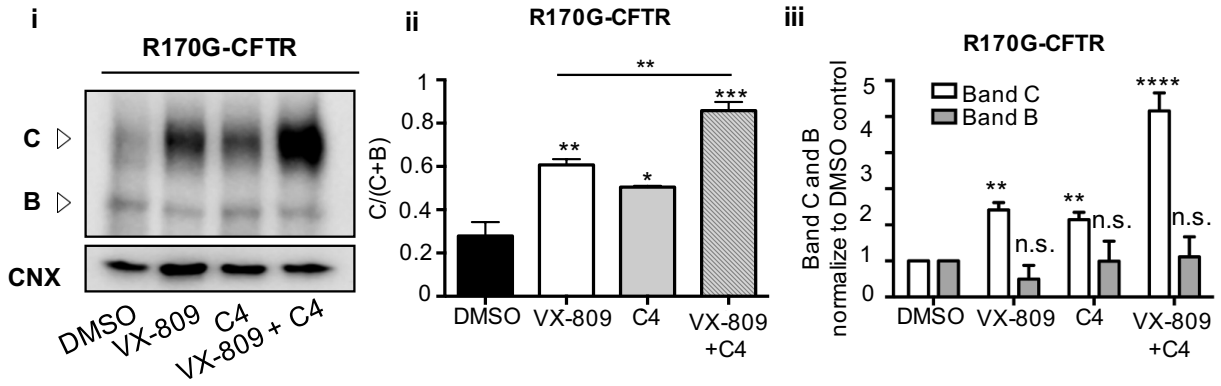

FIGURE S2: Additive effect of VX-809 and C4 on processing of R170G-CFTR. (i) HEK293 cells were transiently transfected with R170G-CFTR mutant and and treated for 24 h at 37 °C with: DMSO, VX-809 (3 μM), and/or C4 (10 μM). C: mature, complex-glycosylated CFTR; B: immature, core-glycosylated CFTR. (**ii**) Bar represent the the mean (±SEM) of the ratio C/(C+B) and are representative of 3 biological replicates (*p<0.05; **p<0.01; ***p<0.001). (**iii**) Bar represent the Band C and band B forms, normalized to DMSO and are representative of 3 biological studies (**p<0.01; ****p<0.0001).

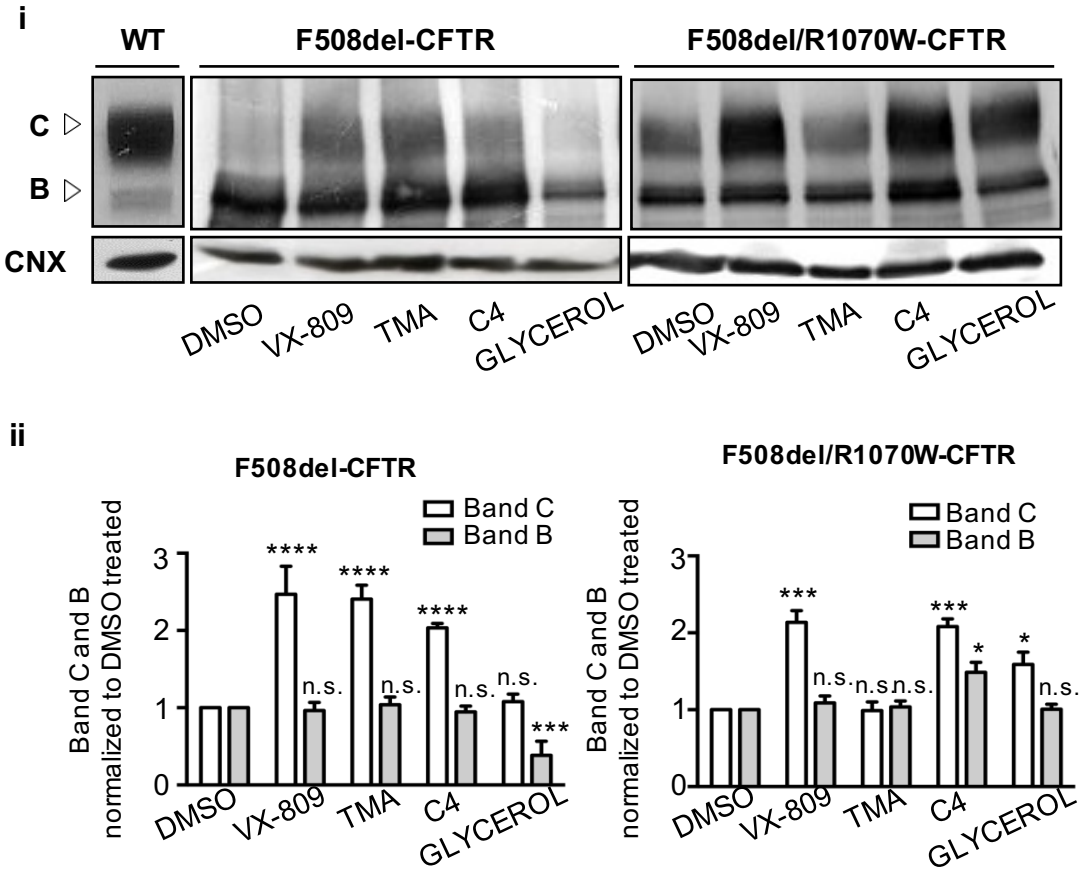

FIGURE S3: VX-809, C4 and glycerol correction of F508del-CFTR is additive with the R1070W second-site mutation. (i) HEK293 cells were transiently transfected with either the F508del-CFTR or F508del/R1070W-CFTR mutant, and treated for 24 h at 37 °C with: DMSO, VX-809 (3 μM), TMA (500 nM), C4 (10 μM), or glycerol (5%). C: mature, complex-glycosylated CFTR; B: immature, core-glycosylated CFTR. (**ii**) Bars represent the mean (±SEM) of band C and B normalized to DMSO control of 4 biological studies (*p<0.05; ***p<0.001; ****p<0.0001).