## SUPPLEMENTAL MATERIAL





**Figure S1.** Fig. 6 D shows a comparison of  $Cd^{2+}$  and ATP-induced currents for different mutants with cysteine-substituting amino acids in or around the signature sequence of NBD1. Here, we show a similar figure, but in this case the  $Cd^{2+}$ -induced currents were compared with the basal current (i.e., current in the absence of ATP). Like Fig. 6 D, this figure also singles out 548–551 as the critical region for mediating  $Cd^{2+}$  effects when they are converted to cysteine. One should note, however, that although this type of analysis may suggest that  $Cd^{2+}$  poses smaller effects on G551C than on L548C and S549C, the fact that the  $Cd^{2+}$ -induced current is approximately sevenfold higher than ATP-induced current (Fig. 6 D) points to the importance of the 551 position in mediating  $Cd^{2+}$  effects.



Figure S2. Fig. 5 shows a comparison of  $Cd^{2+}$  and ATP-induced currents among G551A, G551D, and G551C mutants. Here, the ratio of currents induced by 10  $\mu$ M  $Cd^{2+}$  and those in the absence of ATP (i.e., basal currents) for G551C-, G551D-, and G551A-CFTR are shown. This type of data presentation supports our conclusion that  $Cd^{2+}$  likely interacts directly with the side chain of the amino acid residue at the 551 position.