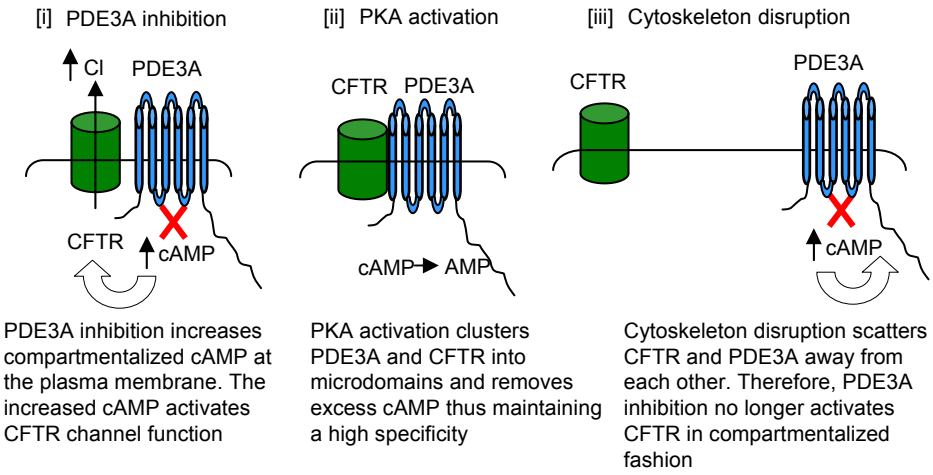
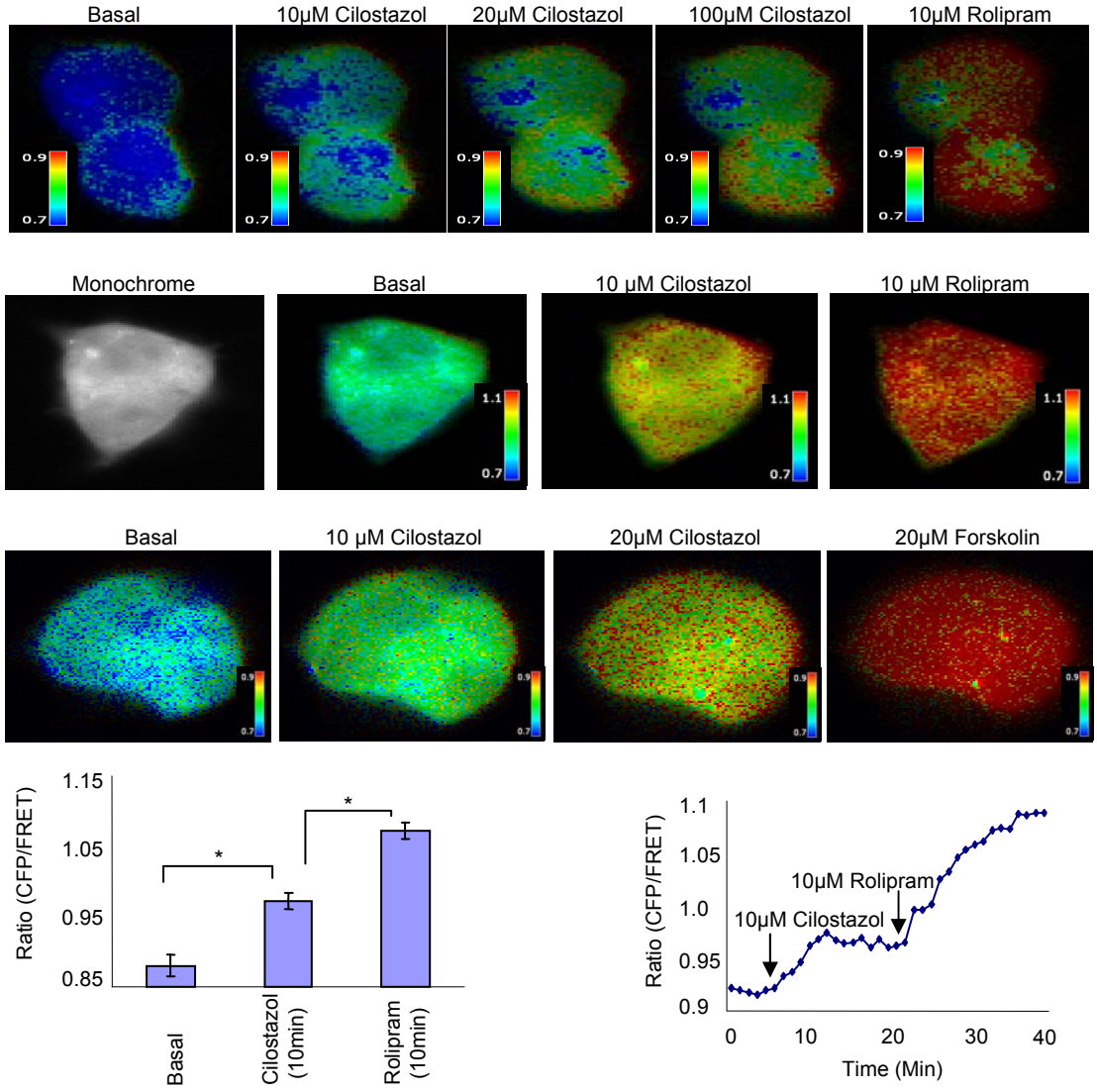
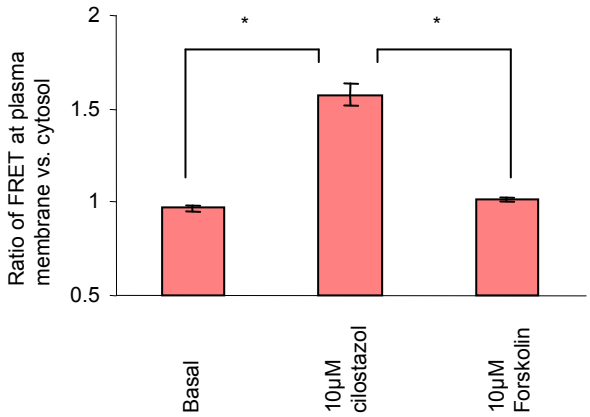


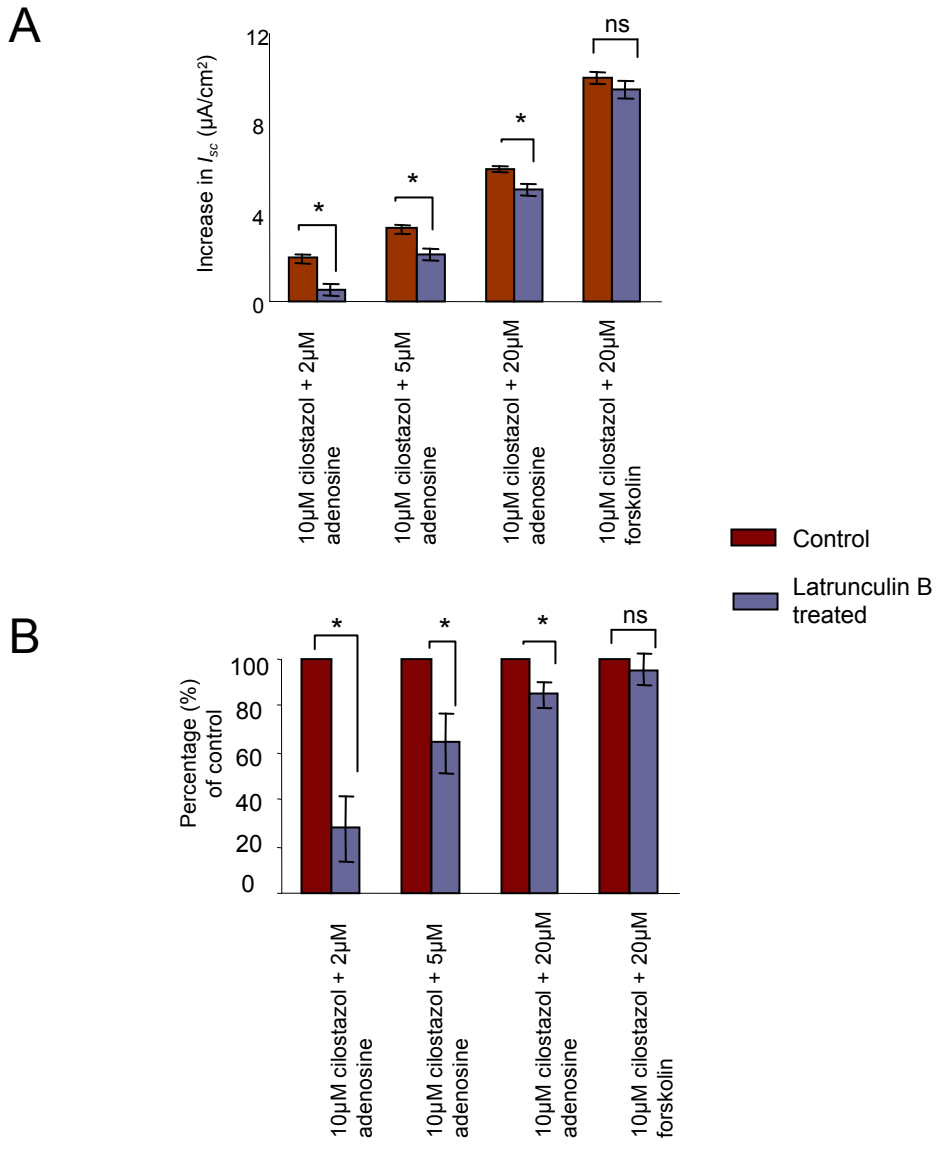
Supplemental Figure S1. Pictorial representation of molecular mechanism of PDE3A coupling to CFTR chloride channel function.



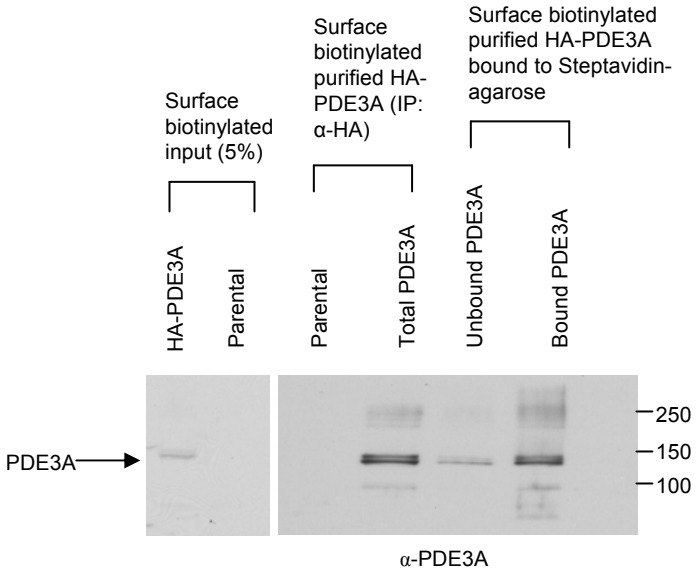
Supplemental Figure S2. Representative pseudocolor images of CFP/FRET emission ratio before (time = 0 min) and after addition of 10-20 μM PDE3 and PDE4 inhibitors cilostazol and rolipram (time = 10 min). Forskolin (20 μM) was added at the end of the experiment to monitor global cAMP response.



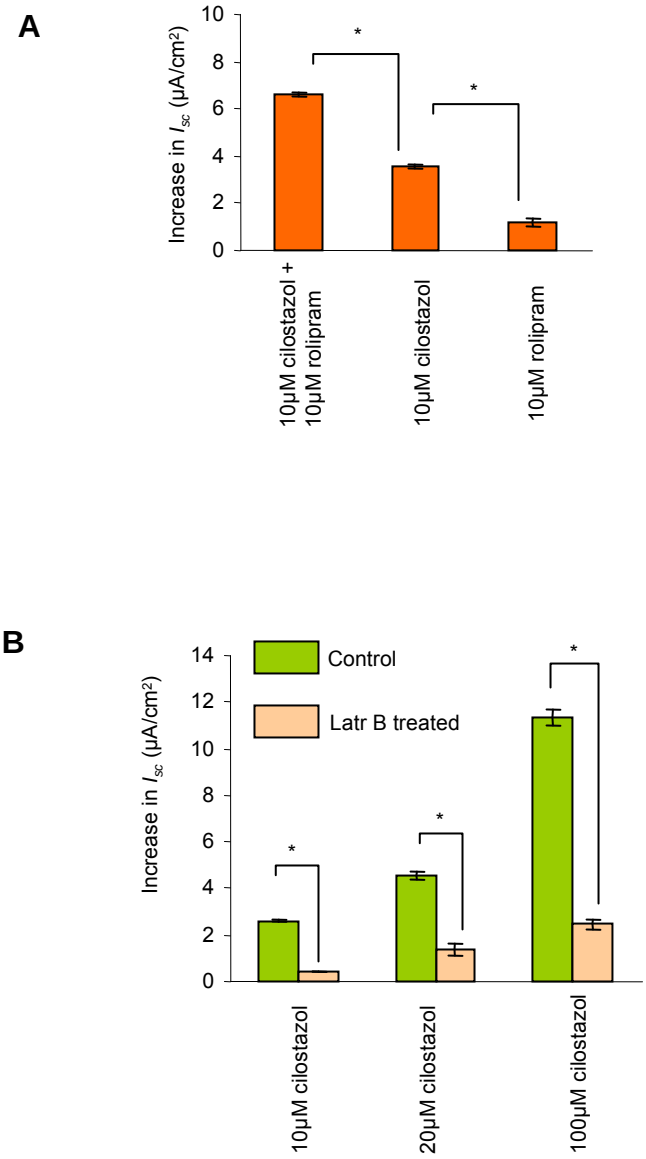
Supplemental Figure S3. Ratio of FRET at the plasma membrane vs. cytosol in Calu-3 cells (mean +/- SEM, n=5, *p<0.001) indicates compartmentalized distribution of cAMP upon PDE3 inhibition



Supplemental Figure S4. (A) Adenosine mediated CFTR short-circuit currents (I_{sc}) in the presence of PDE3 inhibitor cilostazol are significantly inhibited by actin cytoskeleton disruptor latrunculin B (mean +/- SEM, n=3, *p<0.001). (B) The data in Figure S4A is converted to percentage (%) of control where control is taken as maximal 100%. The bar graph shows averaged maximal I_{sc} after lantrunculin B treatment as a percentage of the control. The data shows mean +/- SEM, n=3, ns: not significant. *p<0.001 compared with control for each dose.



Supplemental Figure S5. Immunoblot for PDE3A expression on the plasma membrane of HEK293 cells expressing HA-PDE3A. Bound PDE3A clearly shows that about 90% of PDE3A is present at the plasma membrane.



Supplemental Figure S6. (A) Quantification of Ussing chamber experimental data in Figure 2 (mean +/- SEM, n=3, *p<0.001). (B) Quantification of Ussing chamber experimental data in Figure 7 (mean +/- SEM, n=3, *p<0.001).