Supplementary Materials for

Molecular overlap in the regulation of SK channels by small molecules and phosphoinositides

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Figure S1  The influence of NS309 on the conformation of IDF. (A), A representative snapshot from MD simulations of CaM (salmon) and the SK2-a channel (gray) in the absence of NS309. (B), A representative snapshot from MD simulations of CaM (salmon) and SK2-a channel (gray) in the presence of NS309.

Figure S2  The influence of PIP$_2$ on the conformation of the IDF. (A). The E404-R471 distance from MD simulations in the absence (black) and presence (green) of PIP$_2$. (B), The E404-K75 distance from MD simulations in the absence (black) and presence (green) of PIP$_2$. 

Figure S3  The PIP2-channel interaction is affected by NS309. The histogram of P5-K405 (A), P5-K402 (B), P4-K405 (C), P4-K402 (D) distances from MD simulations in the presence and absence of NS309.
Figure S4  The effectiveness of NS309 on the phosphomimetic T79D CaM mutant.  
(A), Dose-response curves of channel reactivation by exogenous diC₈-PIP₂ in the absence 
(solid line, filled symbols) and presence (dashed line, open symbols) of 3µM NS309, on 
WT/T79D (SK2-a/CaM) mutant channel.  (B), The apparent diC₈-PIP₂ affinity for the 
WT/T79D mutant channel is increased by 3µM NS309.
Figure S5  The proximity of NS309 and CaM T79D mutation to the PIP$_2$ binding site. (A), A representative snapshot from MD simulations of PIP$_2$ binding in the absence of NS309, with the CaM T79D mutation. (B), Summarized probability of forming salt bridges between the PIP$_2$ head and positively charged residues in the absence of NS309, with the WT/T79D (SK2-$\alpha$/CaM) mutant channel. (C), A representative snapshot from MD simulations of PIP$_2$ binding in the presence of NS309, with the WT/T79D mutant channel. (D), Summarized probability of forming salt bridges between the PIP$_2$ head and positively charged residues in the CaM T79D background and in the presence of NS309.
Figure S6  PIP2-channel interaction is affected by NS309 in the context of the T79D mutant. The histogram of P4-K77 (A), P4-K402 (B), P5-K402 (C), P5-K405 (D) distances from MD simulations in the presence and absence of NS309.