

Supplementary Information for

A multiscale approach for bridging the gap between potency, efficacy, and safety of small molecules directed at membrane proteins

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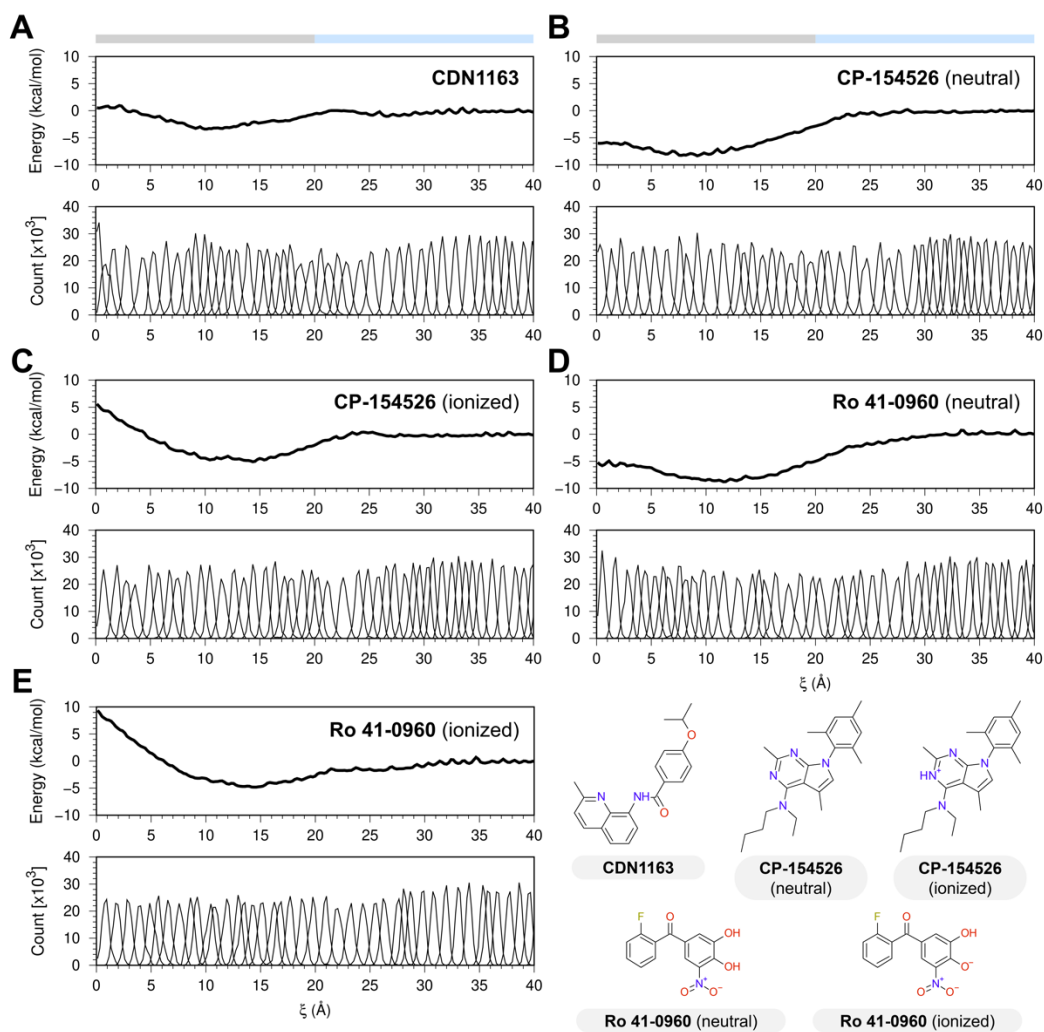


Fig. S1. Umbrella sampling analysis. Potential of mean force (PMF) profile (top) and histograms (bottom) of (A) CDN1163, (B, C) CP-154526, and (D, E) Ro 41-0960 through the POPC lipid bilayer along the reaction coordinate (ξ). The lower right section shows the chemical structures of the compounds and the protonation states used during the study.

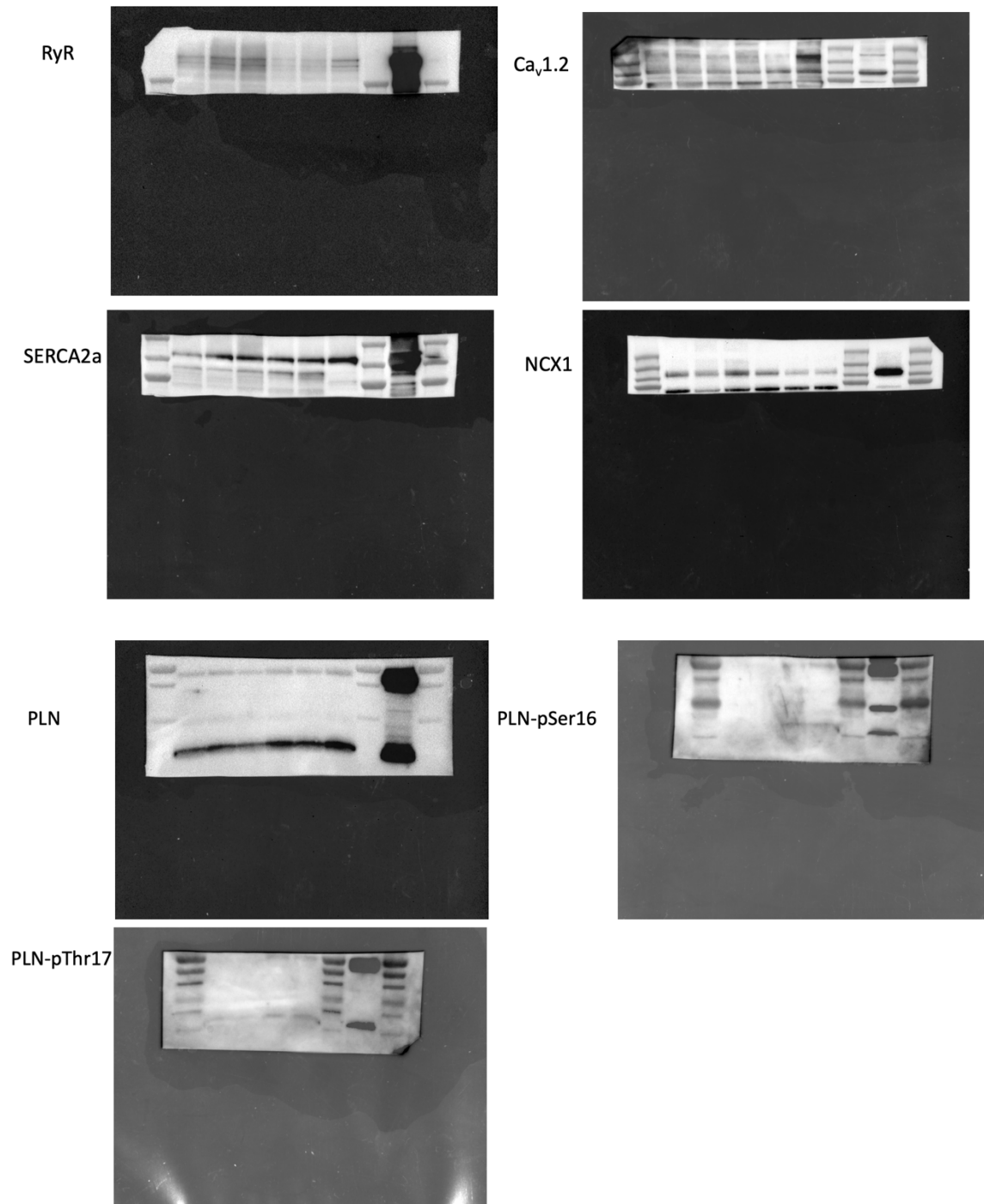


Fig. S2. Original images (tiff format) exported from the Image Lab software (Bio-Rad) obtained by the scanning of blots. For the final Figure 5 in the main text, we crop the black/grey area of each image and adjust the size in a way that all blots have the same length. In some cases, the levels were adjusted so that the bands become more apparent; the whole horizontal lines of bands were adjusted at the same time.

Table S1. Antibodies used to detect and quantify expression of Ca²⁺-handling proteins in iPSC-derived cardiac cells

Primary antibodies	Vendor/Supplier	Catalog #	Dilution
GAPDH	Sigma	G-8785	1:2000
Serca2a	ThermoFisher	MA3-919	1:500
Phospholamban	Badrilla	A010-14	1:5000
Phospho-phospholamban (PLN-Ser16)	Badrilla	A010-12AP	1:2500
Phospho-phospholamban (PLN-Thr17)	Badrilla	A010-13AP	1:1000
Ryanodine Receptor (all RYR)	ThermoFisher	MA3-925	1:500
Cav1.2	Alomone	ACC-003	1:250
NCX1	Swant	R3F1	1:500
Secondary antibodies			
Goat anti-mouse-HRP	Jackson ImmunoResearch	115-035-166	1:1000 1:5000 for GAPDH
Goat anti-rabbit-HRP	Jackson ImmunoResearch	111-035-144	1:1000