Supplementary information

Table S*1* - Descriptors used to select the 22 molecules for experimental validation

SM	Tanimoto	+ ionizable sites	acceptor sites	donor sites	aromaticity
1	0.4444	1	1	0	True
2	0.4737	1	0	0	True
3	0.4857	1	1	0	True
4	0.439	1	0	0	True
5	0.4722	1	1	0	True
6	0.439	1	1	0	True
7	0.4359	1	1	0	True
8	0.1818	5	1	0	True
9	0.0909	1	4	1	True
10	0.5312	1	0	0	True
11	0.4615	1	0	0	True
12	0.4848	1	0	0	True
13	0.1159	1	0	1	True
14	0.325	1	0	1	True
15	0.3333	1	0	1	True
16	0.4474	1	1	1	True
17	0.2391	1	1	0	True
18	0.439	1	1	0	True
19	0.4615	1	0	0	True
20	0.439	1	0	0	True
21	0.4524	1	2	0	True
22	0.5588	1	0	0	True
NAO	1.0	1	0	0	True

Table S2 - Systematic names of the 22 small molecules

SM	Systematic name
1	1-ethyl-6-methoxyquinolin-1-ium iodide
2	3-ethyl-2-[(E)-2-[methyl(phenyl)amino]ethenyl]-1,3-benzoxazol-3-ium ethyl sulfate
3	3-ethyl-5-methoxy-2-methyl-1,3-benzothiazol-3-ium 4-methylbenzene-1-sulfonate
4	3-ethyl-2-[(1E,3E)-4-[methyl(phenyl)amino]buta-1,3-dien-1-yl]-1,3-benzothiazol-3-ium iodide
5	3-(dimethylamino)-5-ethylphenazin-5-ium iodide
6	3-ethyl-5-methoxy-2-[2-(methylsulfanyl)but-1-en-1-yl]-1,3-benzothiazol-3-ium methyl sulfate
7	4-(dimethylamino)-1-[3-(naphthalen-1-yloxy)propyl]pyridin-1-ium chloride
8	3-(4-bromophenyl)-1-(2-oxo-2-phenylethyl)-5H,6H,7H-pyrrolo[1,2-a]imidazol-1-ium bromide
9	4-({[3-(ethoxycarbonyl)-4,5-dimethylthiophen-2-yl]carbamoyl}methyl)-4-methylmorpholin-4-ium chloride
10	1-pentadecylquinolin-1-ium iodide
11	2-[(E)-2-[4-(dimethylamino)phenyl]ethenyl]-1-ethylquinolin-1-ium iodide
12	3-butyl-2-methyl-1,3-benzothiazol-3-ium iodide
13	2-[(1E)-3-[(1E)-5,5-dimethyl-3-[(1E)-3-[(2E)-1,1,3-trimethyl-1H,2H,3H,4H,5H-benzo[e]indol-2-ylidene]prop-1-en-1-yl]cyclohex-2-en-1-ylidene]prop-1-en-1-yl]-1,1,3-trimethyl-1H-benzo[e]indol-3-ium perchlorate
14	2-amino-6-chloro-3-propyl-1,3-benzothiazol-3-ium iodide
15	2-amino-6-methyl-3-propyl-1,3-benzothiazol-3-ium iodide
16	2-amino-6-methoxy-3-propyl-1,3-benzothiazol-3-ium iodide
17	4-[(E)-2-[4-(diethylamino)phenyl]ethenyl]-1-[(4-fluorophenyl)methyl]pyridin-1-ium iodide
18	1-[2-oxo-2-(4-pentylphenyl)ethyl]quinolin-1-ium bromide
19	2-[(E)-2-[4-(dimethylamino)phenyl]ethenyl]-3-ethyl-1,3-benzothiazol-3-ium iodide
20	3-ethyl-2-[(E)-2-[methyl(phenyl)amino]ethenyl]-5-phenyl-1,3-benzoxazol-3-ium bromide
21	3-butyl-2-{[2-oxo-2-(pentyloxy)ethyl]sulfanyl}-1,3-benzothiazol-3-ium bromide
22	3-dodecyl-2-(methylsulfanyl)-1,3-benzothiazol-3-ium methyl sulfate

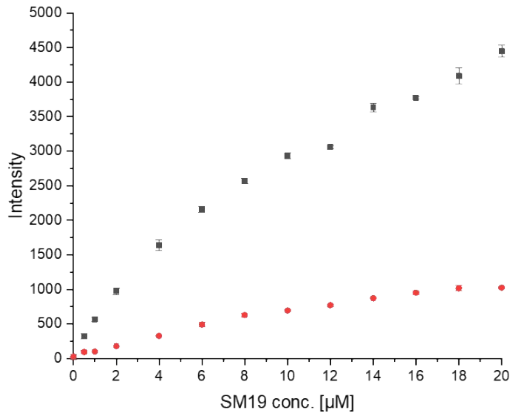

Figure S*1* - Membrane incorporation of SM_{19} in CL-containing E. coli bacteria. The SM_{19} fluorescence emission is affected in presence of E. coli cells. In presence of bacteria (black), the SM_{19} fluorescence emission at 592 nm increases, indicating proper membrane incorporation of the dye.

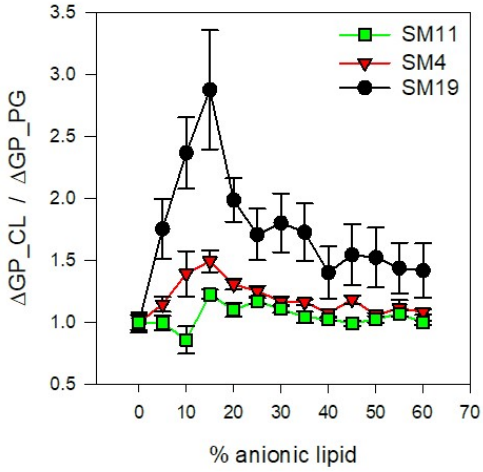

Figure S3 - Ratio between the ΔGP values in DOPC/DOPG and DOPC/CL containing liposomes. The large deviation from constant ratio for SM_{19} clearly indicates the highest specification towards cardiolipin for this molecule.

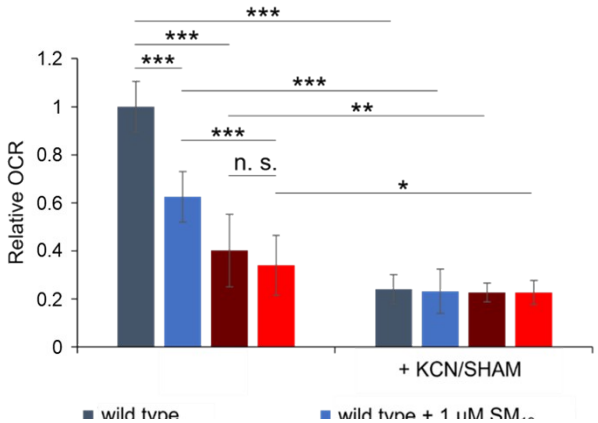

Figure S2 - Oxygen consumption measurements with mitochondria isolated from 6 days old wild-type and *ΔPaCrd1* isolates. Measurements were performed presence vs. absence of 1 µM SM_{19}. The oxygen consumption rate (OCR) in the phosphorylating respiration state (in the presence of ADP) of the wild type was set to 1. In the wild-type, SM_{19} treatment significantly reduces phosphorylating respiration by around 40 % compared to the control. In contrast, addition of SM_{19} had only marginal effects in the mutant. In contrast, upon addition of KCN/SHAM a significant reduction in oxygen consumption was observed, independent of the strain and SM_{19}. (Measurements of the phosphorylating respiration of wild type (n=15), of wild type + 1 µM SM19 (n=8), of ΔPaCrd1 (n=14) and of ΔPaCrd1 + 1 µM SM19 (n=9) and with additional adding KCN/SHAM wild type (n=3), wild-type + 1 µM SM19 (n=4), ΔPaCrd1 (n=4) and ΔPaCrd1 + 1 µM SM19 (n=5); mean values ± standard deviation are shown; significant differences are marked with "*", $p < 0.05$); "**", $p < 0.01$); "***", $p < 0.001$); n. s.: not significant).

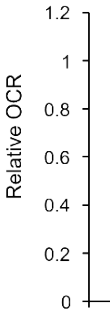

Figure S4 - Oxygen consumption measurements with mitochondria isolated from 6 days old wild-type and *ΔPaCrd1* isolates. Measurements were performed in presence vs. absence of 1 µM SM_{18}. The oxygen consumption rate (OCR) in the phosphorylating respiration state (in the presence of ADP) of the wild type was set to 1. Neither in the wild-type nor in the mutant strain, SM_{18} treatment had a significant impact on phosphorylating respiration. (Measurements of the phosphorylating respiration of wild type (n=15), of wild type + 1 µM SM18 (n=3), of ΔPaCrd1 (n=14) and of ΔPaCrd1 + 1 µM SM18 (n=2); mean values ± standard deviation are shown.