

## Supplemental; Small compounds modulate and bind MscL similarly

**S2 Table. List of free energy components (in kcal/mol) for MM-PBSA binding free energy calculation.  $\epsilon_{lip}$  is the dielectric constant of the lipids.**

System	vdW	EEL	$\Delta G_{pol}^{PB}$			$\Delta G_{nonpolar}^{SAS}$	T $\Delta$ s	Binding		
			$\epsilon_{lip}=1$	$\epsilon_{lip}=2$	$\epsilon_{lip}=4$			$\epsilon_{lip}=1$	$\epsilon_{lip}=2$	$\epsilon_{lip}=4$
Pose 1 Cluster 1	-35.36 $\pm 0.74$	-3.73 $\pm 0.34$	16.31 $\pm 0.30$	15.37 $\pm 0.28$	15.06 $\pm 0.23$	-3.67 $\pm$ 0.03	-19.61 $\pm 0.13$	-6.86 $\pm$ 0.76	-7.79 $\pm$ 0.75	-8.10 $\pm$ 0.70
Pose 1 Cluster 2	-33.91 $\pm 0.71$	-7.03 $\pm 0.46$	19.53 $\pm 0.39$	17.34 $\pm 0.23$	16.39 $\pm 0.29$	-3.59 $\pm$ 0.03	-19.14 $\pm 0.28$	-5.76 $\pm$ 0.58	-8.06 $\pm$ 0.55	-9.01 $\pm$ 0.60
Pose 1 Combined	-34.94 $\pm 0.73$	-4.69 $\pm 0.13$	17.25 $\pm 0.16$	15.93 $\pm 0.14$	15.44 $\pm 0.12$	-3.65 $\pm$ 0.03	-19.47 $\pm 0.17$	-6.55 $\pm$ 0.66	-7.90 $\pm$ 0.62	-8.37 $\pm$ 0.57
Pose 3	-45.64 $\pm 0.17$	-10.86 $\pm 0.36$	18.11 $\pm 0.13$	16.96 $\pm 0.02$	16.69 $\pm 0.03$	-3.61 $\pm$ 0.02	-21.37 $\pm 0.07$	-20.62 $\pm$ 0.24	-21.78 $\pm 0.23$	-22.05 $\pm$ 0.26
Pose 4	-33.55 $\pm 0.09$	-8.18 $\pm 0.19$	21.10 $\pm 0.13$	17.64 $\pm 0.21$	16.37 $\pm 0.26$	-3.49 $\pm$ 0.01	-19.39 $\pm 0.04$	-4.73 $\pm$ 0.20	-8.20 $\pm$ 0.17	-9.47 $\pm$ 0.20