

Discovery of Novel Human Aquaporin-1 Blockers

Daniel Seeliger, Cinta Zapater, Dawid Krenc, Rose Haddoub, Sabine Flitsch, Eric Beitz, Joan Cerda and Bert L. de Groot

Supporting Material

1) Alchemical free energy calculations, Compound 1

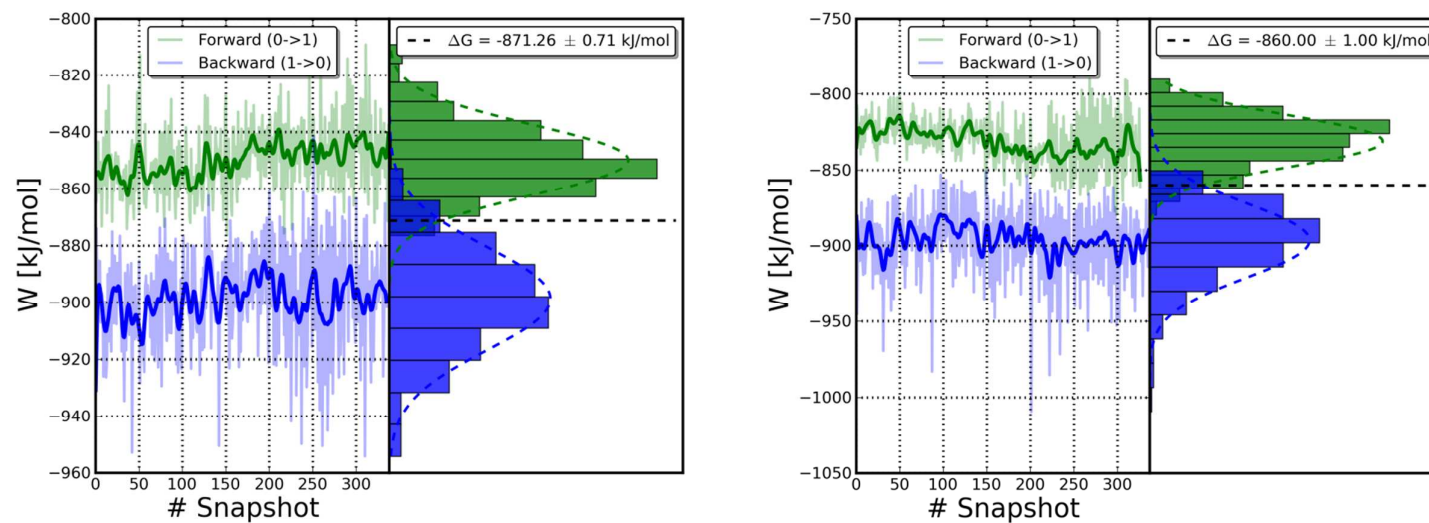


Figure S 1: Results from free energy calculations. Left: K36A mutations in apo-hAQP1. Right: K36A mutation in hAQP1 in complex with compound 1

Result: $\Delta\Delta G = -860.0 - (-871.26) = 11.26$ kJ/mol

2) Alchemical free energy calculations, Compound 2

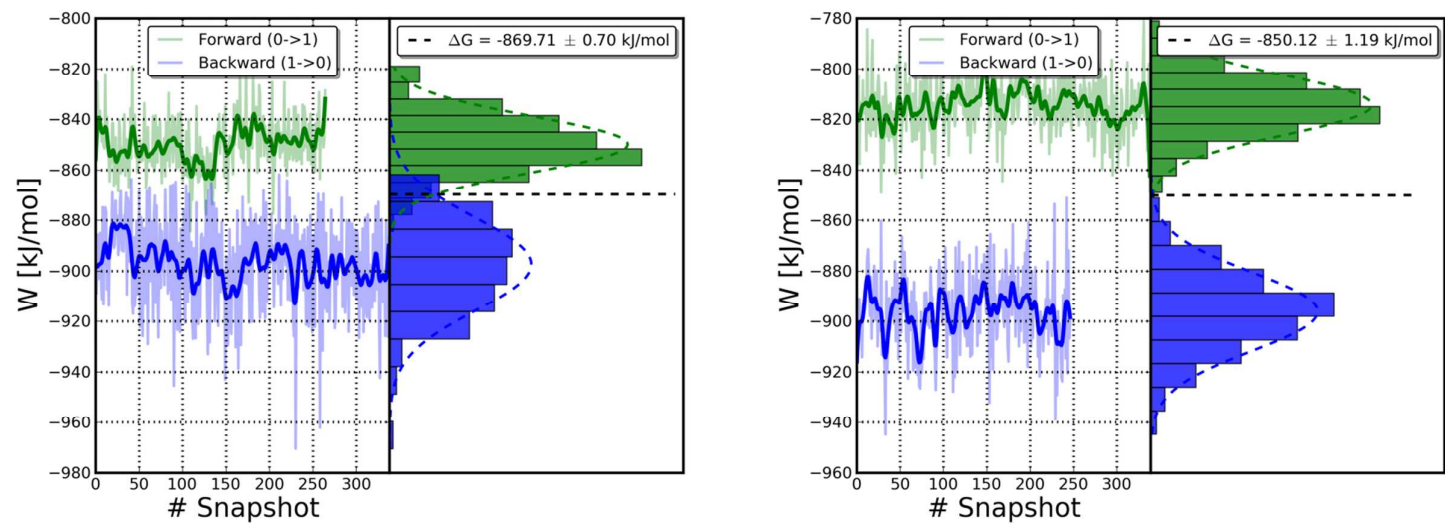


Figure S 2 Results from free energy calculations. Left: K36A mutations in apo-hAQP1. Right: K36A mutation in hAQP1 in complex with compound 2

Result: $\Delta\Delta G = -850.12 - (-869.71) = 19.6 \text{ kJ/mol}$

3) List of tested compounds

SMILES	CATALOG_NUMBER	SUPPLIER_NAME	Result	IC50[μ M]	Synonym
<chem>OC(=O)C=Cc1cccc(C=CC(O)=O)c1</chem>	5310510	ChemBridge	ACTIVE	8.5	Compound 1
<chem>CC(=C/C(O)=O)C(=Cc1ccc2ccccc2n1)C(O)=O</chem>	5571689	ChemBridge	ACTIVE	17.0	Compound 2
<chem>S=C(NCc1ccc2OCOc2c1)Nc1ccc2nsnc2c1</chem>	7027127	ChemBridge	ACTIVE	17.5	Compound 3
<chem>CC(=O)Nc1nnc(s1)S(N)(=O)=O</chem>	L07562	Alfa Aesar	ACTIVE	5.5	Acetazolamide
<chem>OC(=O)CNc1ncnc2c3ccccc3oc12</chem>	5314403	ChemBridge	ACTIVE	107	
<chem>Fc1ccc(NC(=S)Nc2ccc3nccnc3c2)cc1</chem>	7855270	ChemBridge	NO EFFECT	NA	
<chem>OC(=O)c1cccc(Nc2nc(cs2)-c2ccncc2)c1</chem>	5752164	ChemBridge	NO EFFECT	NA	
<chem>CNC(=O)NC(=O)CNc1cccc(c1)C(F)(F)F</chem>	Z88912237	Enamine	NO EFFECT	NA	
<chem>NC(=O)c1ccc(Nc2ccc(F)cc2)c(c1)[N+][O-]=O</chem>	Z31201593	Enamine	NO EFFECT	NA	
<chem>OC(=O)c1ccc(cc1C(O)=O)C(=O)c1ccccc1</chem>	STK388312	Vitas M Labs	NO EFFECT	NA	
<chem>Nc1c(nnn1-c1cccc(F)c1)-c1nc2ccccc2[nH]1</chem>	STK779833	Vitas M Labs	NO EFFECT	NA	
<chem>NC(=O)c1ccccc1NC(=O)c1ccccc1C(O)=O</chem>	STK043603	Vitas M Labs	NO EFFECT	NA	
<chem>Fc1ccccc1NC(=O)Nc1nnc(s1)-c1ccco1</chem>	STK011951	Vitas M Labs	NO EFFECT	NA	
<chem>Fc1ccccc1C(=O)NNc1nc2ccccc2s1</chem>	STK868337	Vitas M Labs	NO EFFECT	NA	
<chem>Nc1ccc2[nH]c(nc2c1)-c1ccccc1C(O)=O</chem>	STK372478	Vitas M Labs	NO EFFECT	NA	