	Sir2 (1YC2 Chain B)	SIRT3 (3GLT)
MM-GBSA *Δ*G Bind with MCMM [b]	-30.0	-14.0
MM-GBSA *Δ*G Bind [c]	-97.0	-77.2
Complex Energy	-12135.3	-11346.4
Ligand Energy (single conformation)	-40.87	-44.8
Ligand Energy (MCMM ensemble)	-107.87	-108.0
Receptor Energy	-11997.4	-11224.4
Original protein conformation	-11242.5	-11592.0

[a] Template-based induced fit (MM-GBSA flexible protein within 5Å) was used for both Sir2 and SIRT3 docking studies. It started with sampling protein degrees of freedom in the presence of ligand, which reduced the apoprotein energy of Sir2. This is a relaxation energy due to protein preparation and is not associated with the binding event.

[b] MM-GBSA *Δ*G Bind with MCMM uses an ensemble of conformations to estimate the free ligand energy.

[c] MM-GBSA *Δ*G Bind refers to score from induced fit docking of NAD^+ to the protein receptor structure produced by sampling backbone and side chain degrees of freedom of the original protein conformation according to the template-based induced fit protocol described in Methods. A single free ligand conformation is used.

Table 1