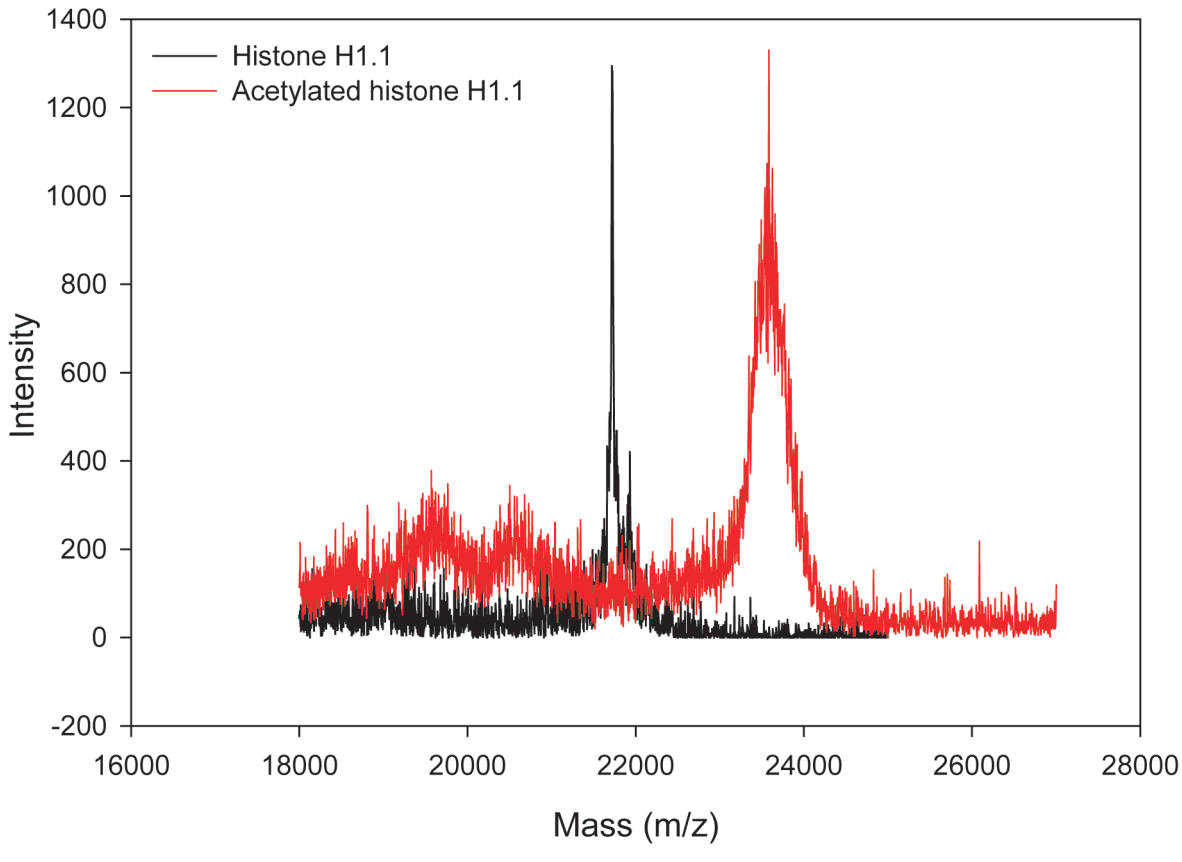

Fig. S1. MALDI mass spectrometry confirms the chemical acetylation of histone H1.1. The acetylation reaction produced a mass shift consistent with the addition of ~46 acetyl groups.

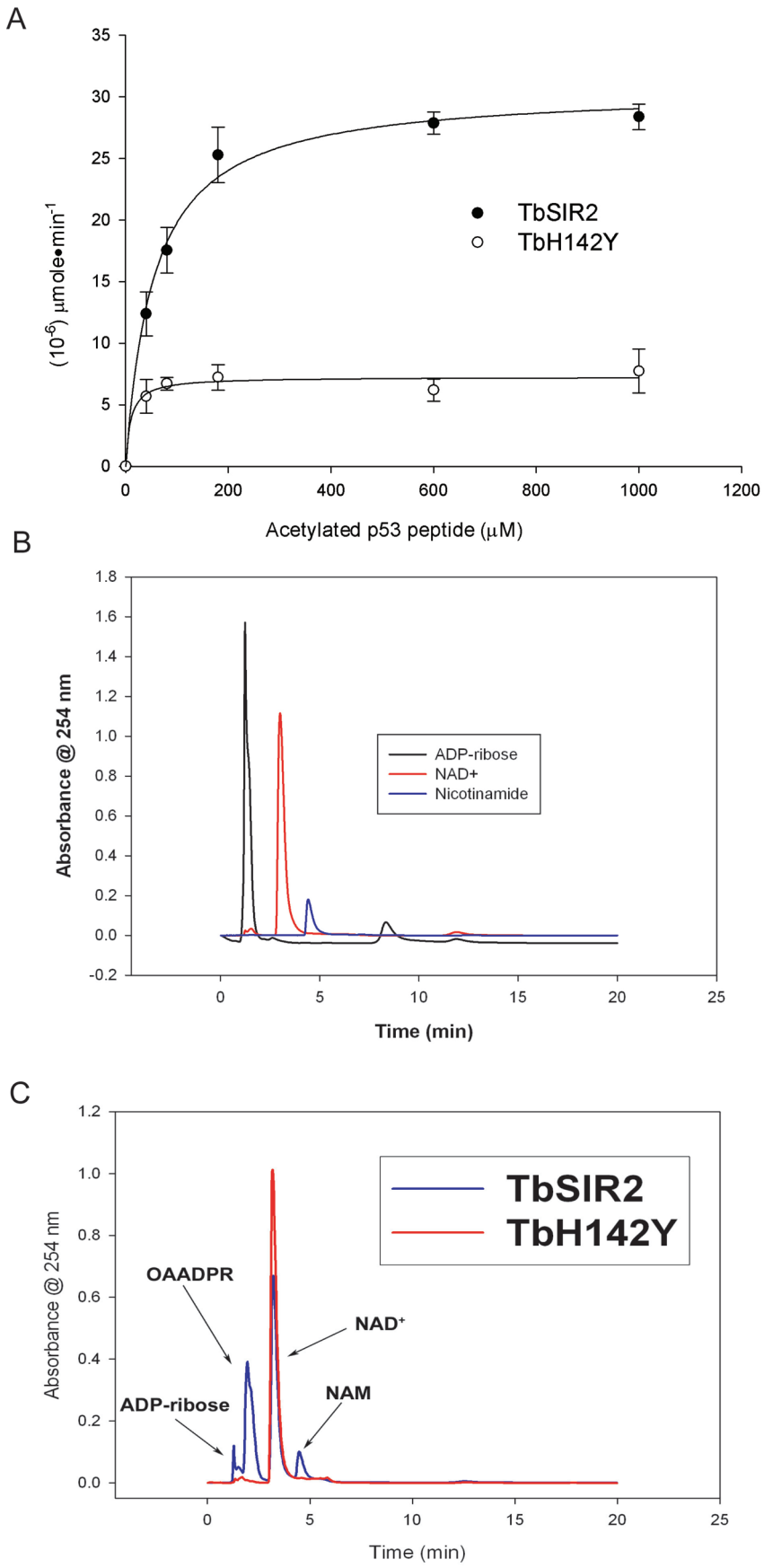

Fig. S2. TbSIR2 can deacetylate chemically acetylated histone H1.1. (A) The deacetylase activity of TbSIR2 and the histidine mutant, TbH142Ywas monitored using an acetylated p53 peptide. (B) HPLC profiles of nicotinamide, NAD+ and ADP-ribose. (C) Chemically acetylated histone H1.1 was tested as a deacetylation substrate with TbSIR2 and TbH142Y. The reactions were analyzed by HPLC for generation of the nicotinamide, OAADPR and ADP-ribose.

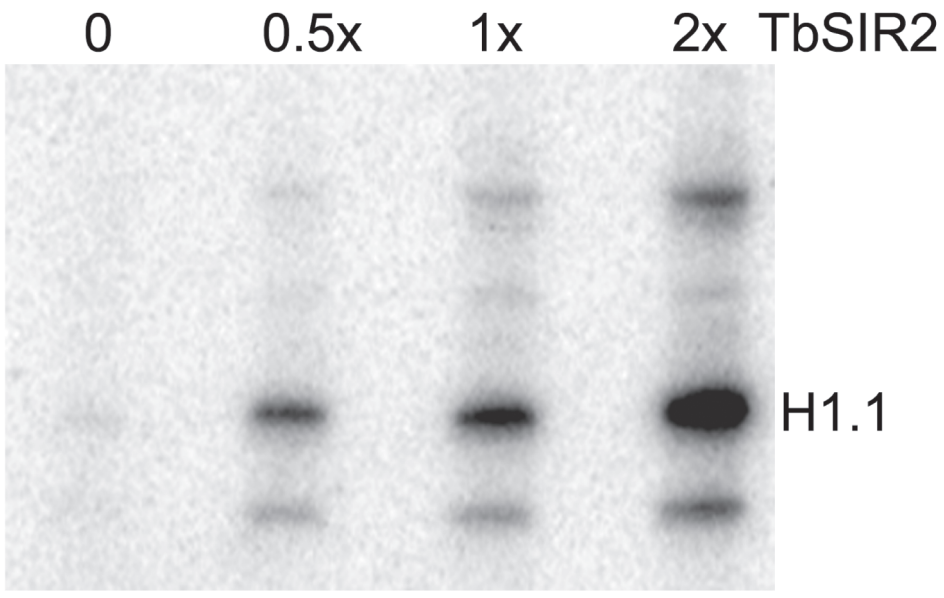

Fig. S3. ADP-ribosylation of unacetylated histone H1.1 is dependent on the concentration of TbSIR2. The radioactive reactions were carried out with TbSIR2 concentrations of 0, 0.3, 0.6 and 1.2 uM.

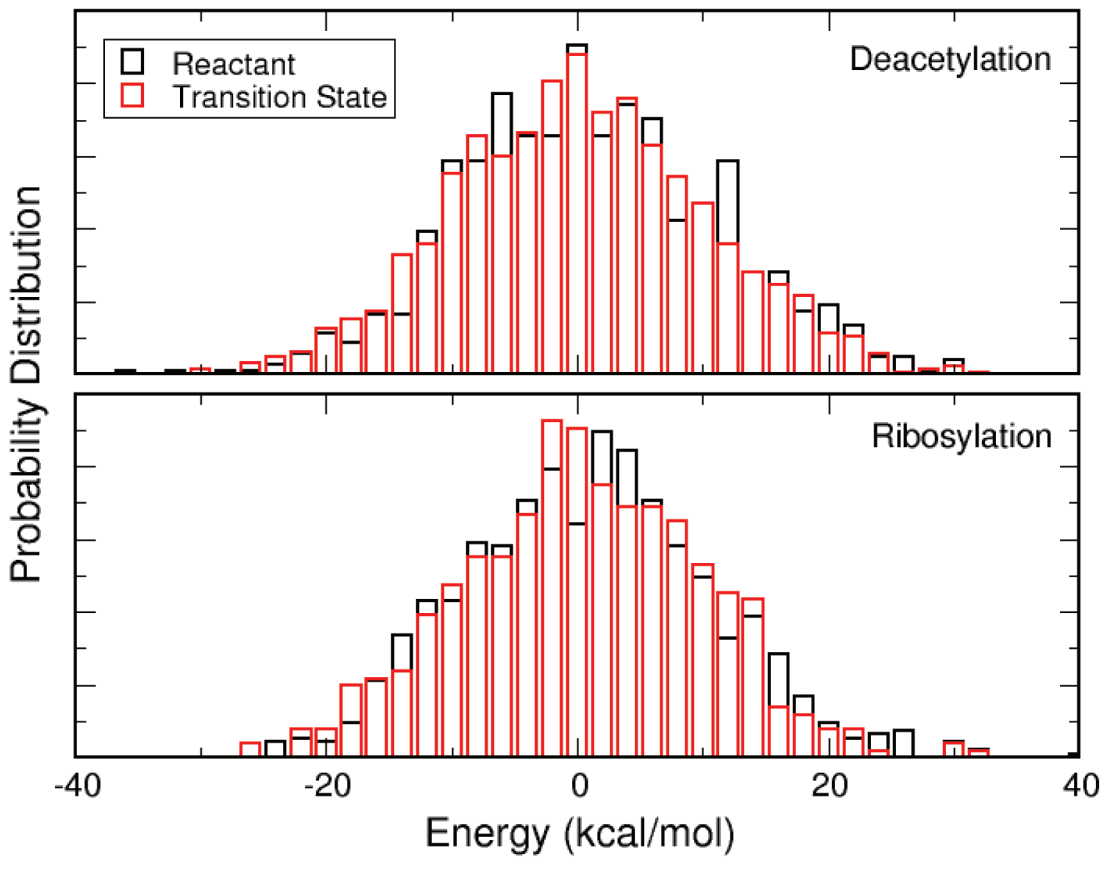

Fig. S4. Calculated enzyme contributions to QM subsystem at reactant (shown in black) and transition state (shown in red) of the nicotinamide cleavage step for deacetylation and ADP-ribosylation.