

**Figure S3.** ITC measurements of DNA binding affinities in the presence of NAD cofactors. The CLOCK-BMAL1 bHLH heterodimeric proteins were titrated into a 16 bp canonical E-box DNA (WT DNA) in the presence of 10 mM NAD cofactors indicated above each plot.  $K_D \pm s.d.$  is shown. Although the  $K_D$  values are slightly different in the presence of different NAD cofactors, neither of them exerts a significant influence on DNA binding.