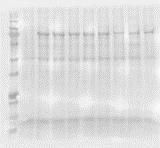


**A.**



**Figure 4- figure supplement 1**



**I219A**

**D190W**

**W188A**

**H133Y**

**D63Y**

**D63H**

**A13W**

**WT**

**-**

**B.**

**C.**

**D.**

**Figure 4- figure supplement 1**

**(A)** List of generated SIRT6 point mutations in the SIRT6 tunnel structure. **(B)** Ponceau staining of SIRT6-MBP point mutants. **(C)** SIRT6-MBP mutants catalytic activity, assessed by H3K9 de-myristolation in a FLUOR DE LYS assay. **(D)** His-tagged mammalian Sirtuins DNA binding ability of circular and linear plasmids. Log of averages of 4-7 experiments +/- SEM (\*=p<0.05, \*\*=p<0.005, \*\*\*=p<0.0005).