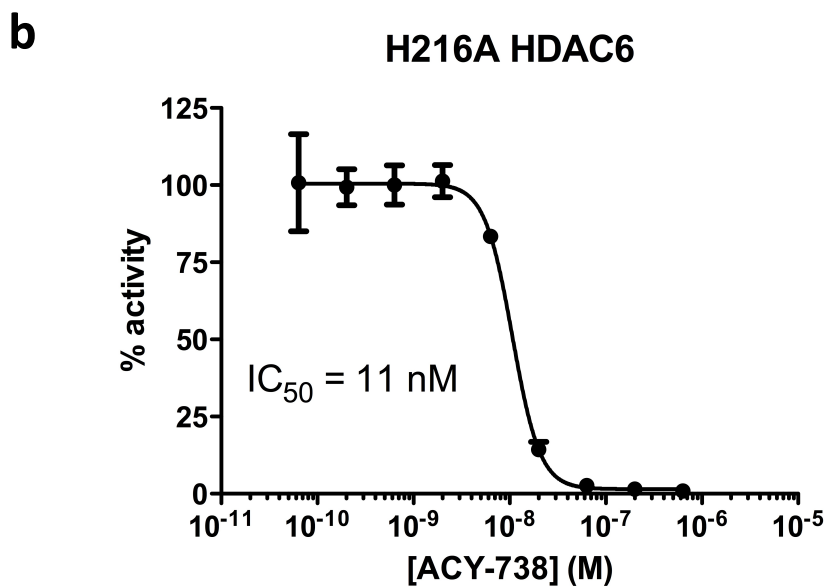
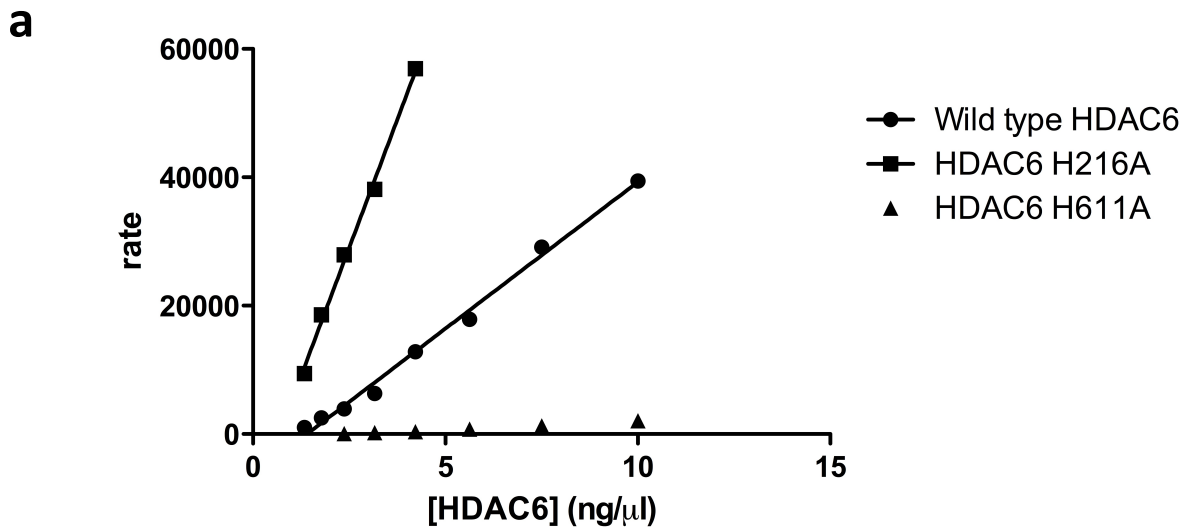


Supplemental Figure 1



(a) Rate of deacetylase activity of HDAC 6 with mutations of C- (H611) and N-terminal (H216) catalytic domains compared to wild-type HDAC6. Mutation of histidine 611 to alanine (H611A) completely abolishes HDAC6 deacetylase activity, while mutation of histidine 216 to alanine (H216A) is still active, showing that the C-terminal domain is completely responsible for the deacetylase activity of HDAC6. (b) ACY-738 is still able to fully inhibit HDAC6 with N-terminal catalytic mutation, indicating that inhibition of the C-terminal domain is responsible for the activity of ACY-738 mediated HDAC6 inhibition.