



**Fig. S3.** ETD fragment ion graphs of Methyl Equivalents from 1 to 10 in H3.3 variant of MMSET-Low cells. Averaged ETD MS<sup>2</sup> spectral intensities from all matched c ions were plotted with absolute intensity in y-axis and cleavage sites in x-axis. Color bars represent different combinatorial modifications of methylation and acetylation from data base search. Most modification pattern (represented by color patterns) changes occurred in  $c_9 - c_{27}$  region in Methyl-Eqs 1 to 4, and  $c_9 - c_{36}$  region in Methyl-Eqs 5 to 10. One acetylation was observed in Methyl-Eqs 6 to 8 and two acetylations in Methyl-Eqs 9 and 10. Black arrows pointing to  $c_8$  ion in Methyl-Eq 2 and 3 indicate no modification and red arrows represent one methyl group in  $c_8$  ion.