

Supplemental Fig. S5. Two examples illustrating how comparisons of DHM_{d-u} between dosage sensitive (DS) and dosage insensitive (DI) ortholog sets were conducted after controlling for bias in the intrinsic histone modification status of the two groups (see Supplemental Fig. S8) (**A-C**, worm H3K79me2, active mark; **B-D**, worm H3K27me3, repressive mark). (**A**)(**D**) The sample sizes of the DS and DI ortholog sets in each bin were categorized according to the level of focal histone modification. The same numbers of samples were taken from each bin of the two groups and these numbers are indicated in bold font. (**B**)(**E**) The distributions of DHM_{d-u} for the DS and DI groups were based on 10,000 bootstrapped samples. (**C**) and (**F**) show the distribution of DHM_{d-u} before controlling for the default histone modification status. (**B**) and (**E**) follow *Predicted Patterns III* and they are consistent with (**C**) and (**F**), respectively. *P*-values were determined with the Mann-Whitney *U*-test.

