

Supplementary Data

Supplementary Figure S1 – An illustration of aligned domain sequences for four families. MUSCLE was used for the alignment (34).

Supplementary Figure S2 – The prediction performances of the HMM identifications. The receiver operating characteristic (ROC) curves were drawn and area under ROC values were calculated for the self-consistency (Curves & triangles in blue) and leave-one-out (Curves & squares in red) validations, respectively. (A) Eight acetylation families, including three HAT families such as p300_CBP, GCN5 and MYST, four HDAC families such as SIR2, Class-I, Class-II and Class-IV, and one Ac_Reader family of Bromodomain. (B) Eight methylation families, including three HMT families such as SET1, SET2 and SUV39, three HDM families such as PHF2_PHF8, JARID and JHDM3_JMJD2, and two Me_Reader families such as Chromodomain and TTD.

Supplementary Figure S3 – The heatmap of the numbers of HATs, HDACs, Ac_Readers, HMTs, HDMs and Me_readers in 68 animals, 39 plants and 41 fungi. Although animals generally have more readers than writers and erasers, the numbers of histone modification enzymes and readers are similar in plants and fungi.

Supplementary Figure S4 – The search and advance options. (A) The WERAM database can be searched with one or multiple keywords; (B) Batch search permits users to input multiple gene names or accession numbers in a line-by-line format for querying (≤ 100); (C) Advance search allows users to query with more than one terms; (D) The option of Histone regulator detection scans protein sequences (≤ 10) in FASTA format using pre-constructed HMM profiles; (E) Blast search option can be used for detecting identical or homologous sequences.

Supplementary Table S1 – The data statistics of known HATs, HDACs, Ac_Readers, HMTs, HDMs and Me_readers collected from the scientific literature.

Supplementary Table S2 – The detailed parameters including log-odds likelihood scores and E-

values used for the hmmsearch program together with numbers of positive and negative proteins in the testing data set.

Supplementary Table S3 – The detailed classification of histone regulator families, together with the numbers of identified members in 148 eukaryotes. Totally, acetylation and methylation regulators were classified into 15 and 32 families, respectively.

Supplementary Table S4 – A comparison of WERAM to dbHiMo, which mainly focused on the identification of histone-modifying enzymes in fungi (27). For eight eukaryotic organisms including *H. sapiens*, *M. musculus*, *R. norvegicus*, *D. melanogaster*, *C. elegans*, *A. thaliana*, *S. pombe* and *S. cerevisiae*, WERAM totally collected and identified 1260 histone regulators, whereas dbHiMo only contained 168 histone-modifying enzymes.