Figure S1. Related to Figure 1.

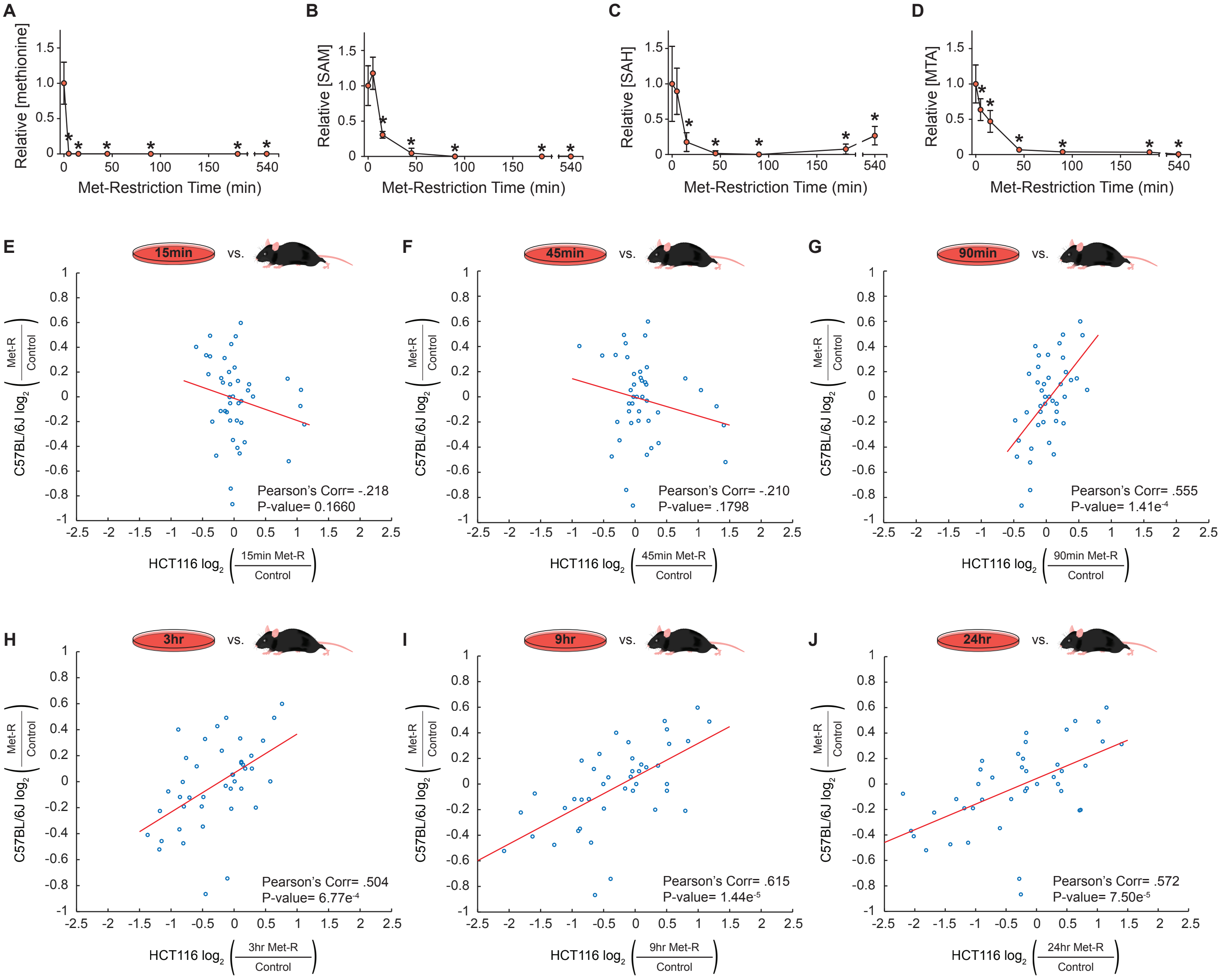


Figure S1: (*A-D*) Scatter plots of relative abundance values for key Met-cycle metabolites in HCT116 cells as measured by LC-MS. n=5, error bars represent SD, *$p<0.05$ (Welch's t-Test). (*E-J*) Correlation plots of LC-MS/MS generated log2 fold-change stoichiometric values for individual histone H3 peptide proteoforms. n≥3. See also Table S1.

Figure S2. Related to Figure 2.

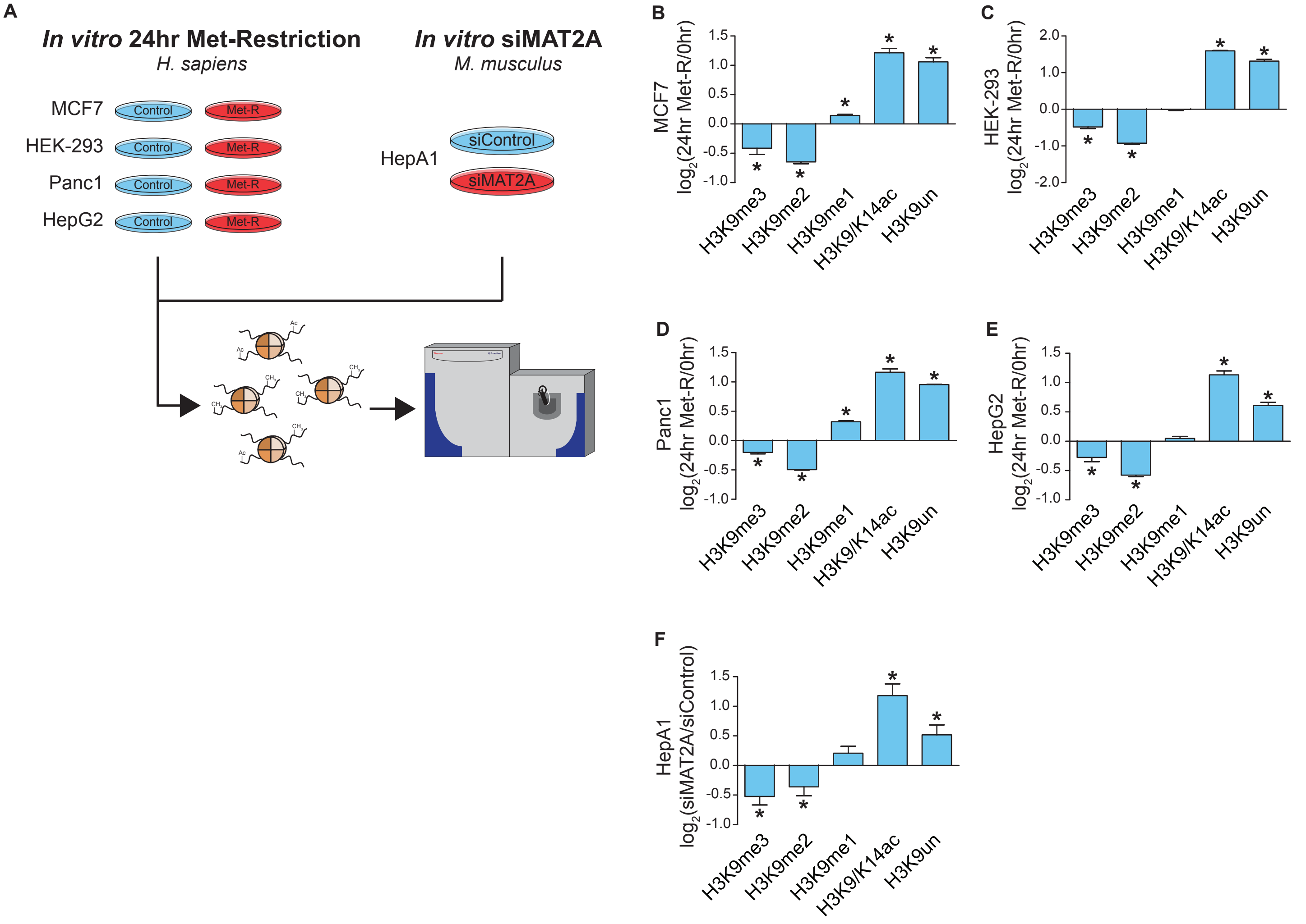


Figure S2: (*A*) Diagram illustrating the experimental design for determining the conservation of H3K9 regulation in response to SAM depletion across various biological systems. (*B-F*) Bar graphs illustrating log2 fold-changes for individual H3K9 in response to in vitro SAM depletion. n=3, error bars represent SD, *p<0.05 (Welch's t-Test). See also Table S1.

Figure S3. Related to Figure 3.

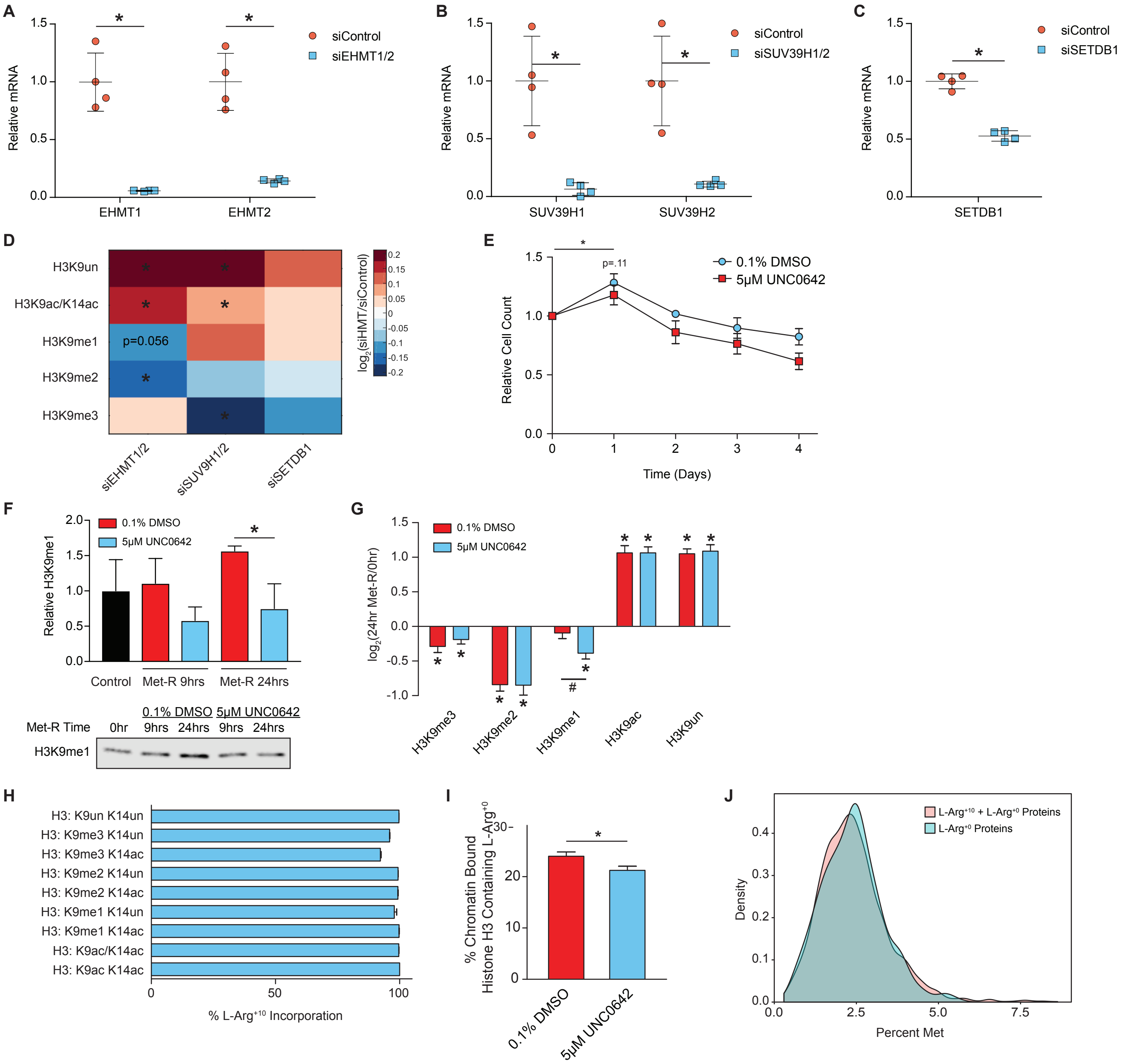


Figure S3: (*A-C*) Scatter plots of relative HMT mRNA abundance in HCT116 cells as measured by RT-qPCR. n=4, error bars represent SD, *p<0.05 (Welch's t-Test). (*D*) Heatmap of log2 fold-change stoichiometric values for unique histone H3K9 peptide proteoforms in HCT116 cells. n=4, *p<0.05 (Welch's t-Test). (*E*) Scatter plot of relative cell counts for attached HCT116 cells. n=4, error bars represent SD, *p<0.05 (Welch's t-Test). (*F*) Bar graph of relative H3K9me1 abundance in HCT116 cells as measured by western blot with accompanied representative blot image. See Data S1 for REVERT Total Protein Stain image used for normalization. Error bars represent SD, n≥3, *p<0.05 (Welch's t-Test). (*G*) Bar graphs illustrating log2 fold-changes for individual H3K9 PTMs. n≥3, *p<0.05 (Welch's t-Test) within PTM, #p<0.05 (Welch's t-Test) across PTMs. (*H*) Bar graph showing average incorporation of L-Arg+10 in H3K9 peptide proteoforms. n=4, error bars represent SD. (*I*) Bar graph illustrating contribution of newly synthesized histone H3 to the total chromatin bound pool after 24 hours of Met-restriction in HCT116 cells as measured by LC-MS/MS. n≥3, error bars represent SD, *p<0.05 (Welch's t-test). (*J*) Density plot illustrating the percentage of Met residue frequency in the primary amino acid sequence of all identified cytoplasmic proteins as well as those determined to be preferentially translated. See also Table S1, Table S2, and Table S3.

Figure S4. Related to Figure 6.

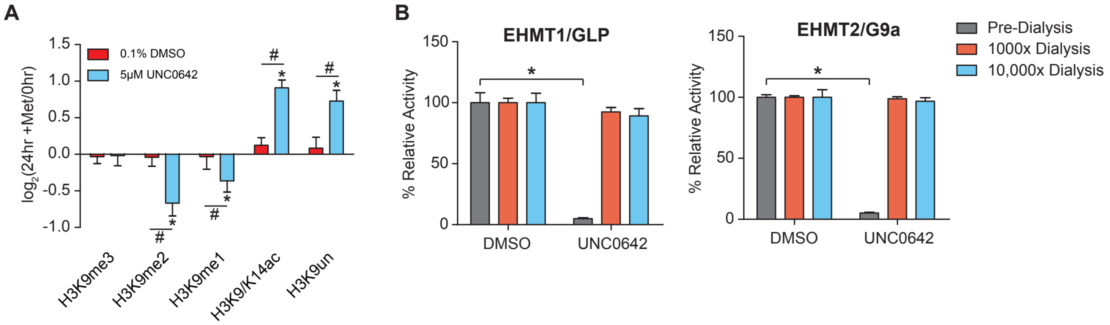


Figure S4: (*A*) Bar graphs illustrating log2 fold-changes for individual H3K9 PTMs 24 hours following UNC0642 removal. n=4, error bars represent SD, *p<0.05 (Welch's t-Test) within PTM, #p<0.05 (Welch's t-Test) across PTMs. (*B*) Bar graphs illustrating relative recombinant enzyme activity in the presence of saturating amounts UNC0642 and following 1000x or 10,000x overnight dialysis. n=4, error bars represent SD, *p<0.05 (Welch's t-Test).

Figure S5. Related to Figure 6.

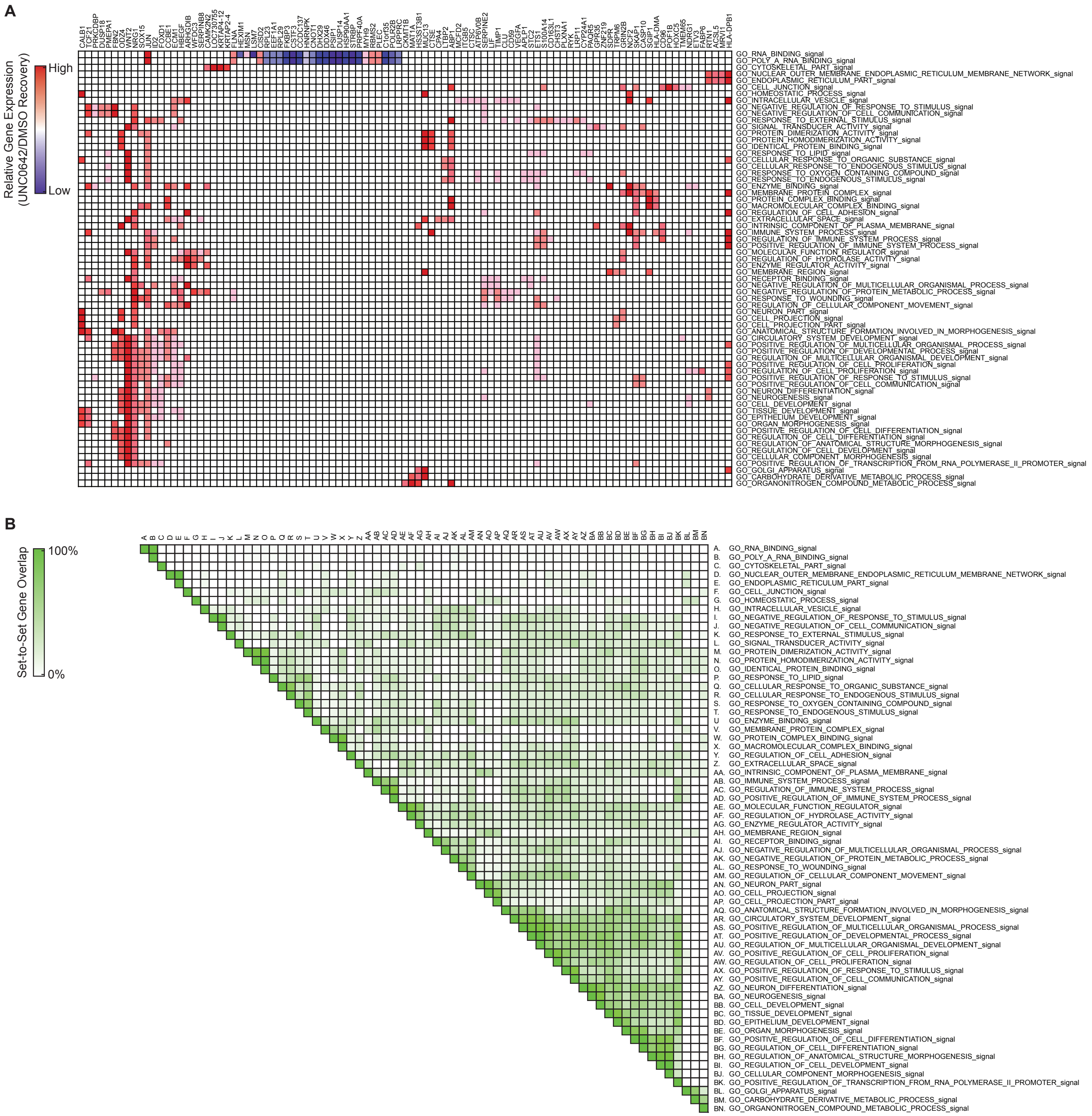


Figure S5: (*A*) GSEA heatmap of relative gene expression across positive NES GO terms identified when comparing UNC0642- to mock-recovery transcripts. (*B*) GSEA set-to-set heatmap illustrating gene enrichment overlap across positive NES GO listed in panel A. See also Table S4 and Table S5.

Figure S6. Related to Figure 6.

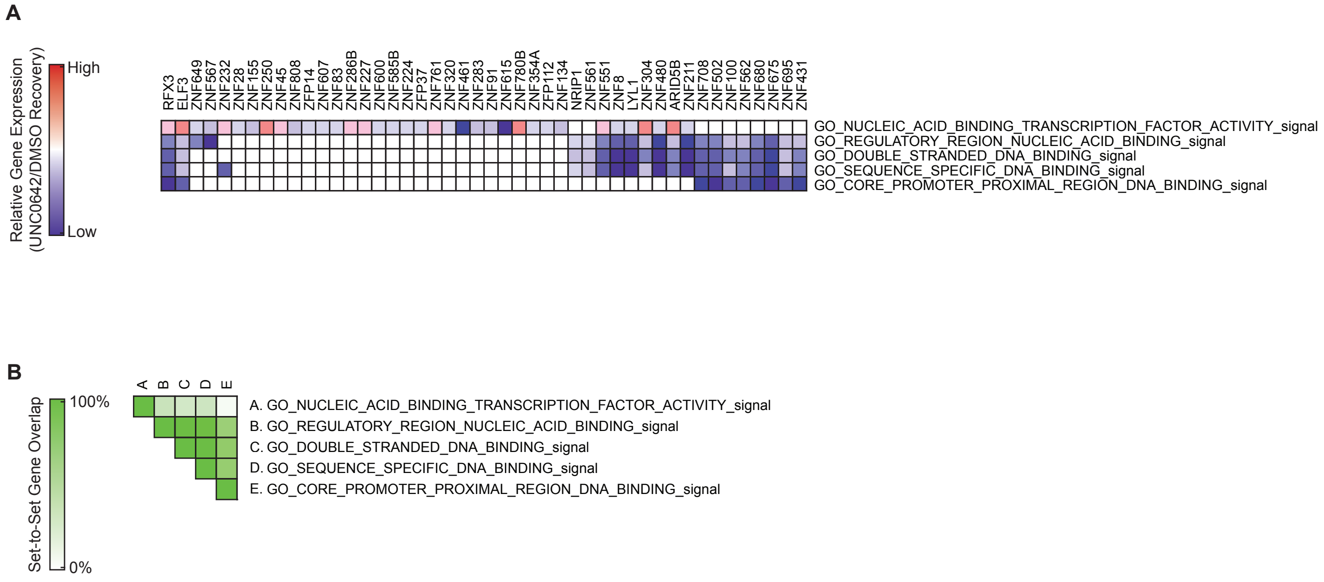


Figure S6: (*A*) GSEA heatmap of relative gene expression across negative NES GO terms identified when comparing UNC0642- to mock-recovery transcripts. (*B*) GSEA set-to-set heatmap illustrating gene enrichment overlap across negative NES GO terms listed in panel A. See also Table S4 and Table S5.

Figure S7. Related to Figure 7.

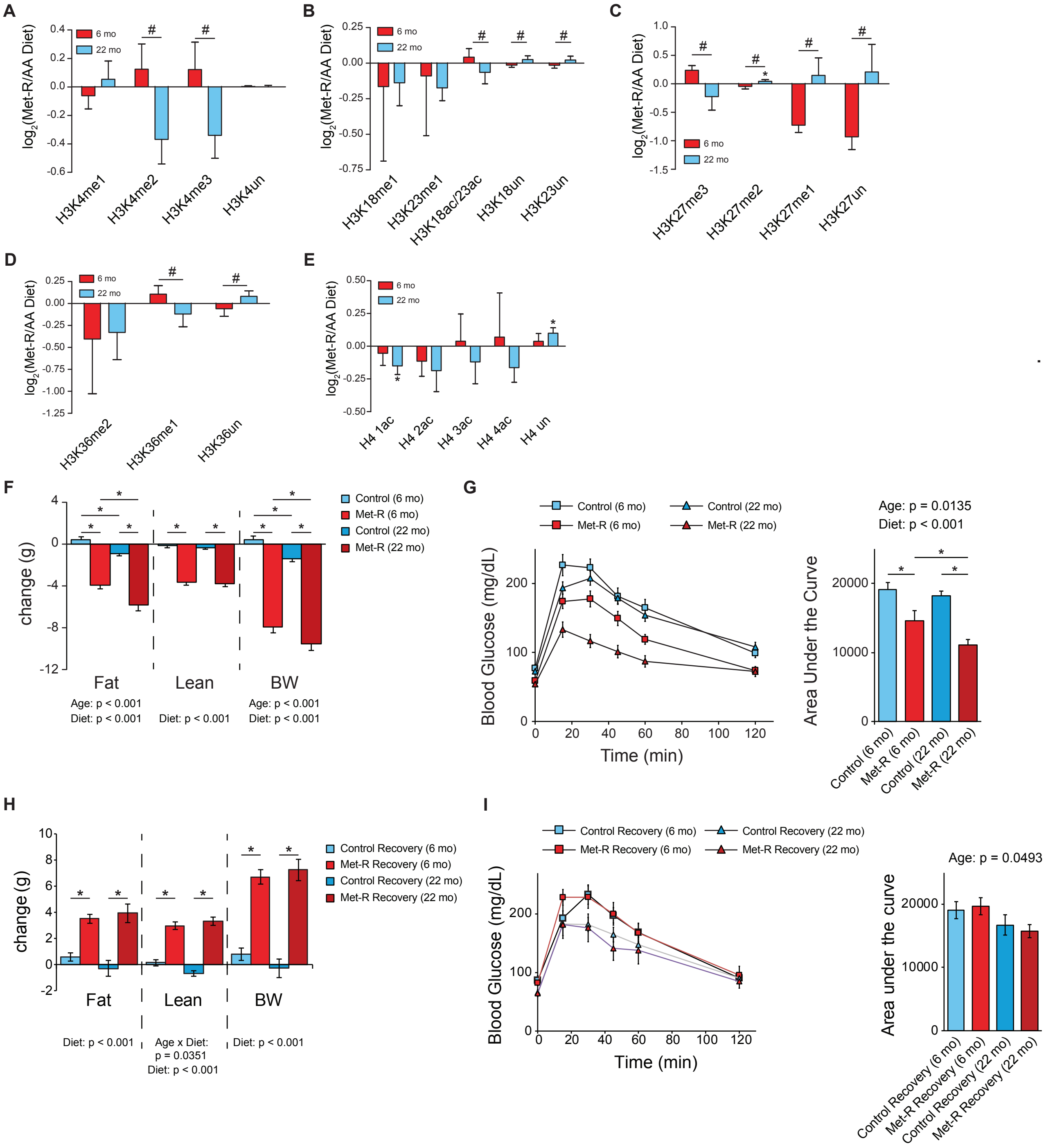
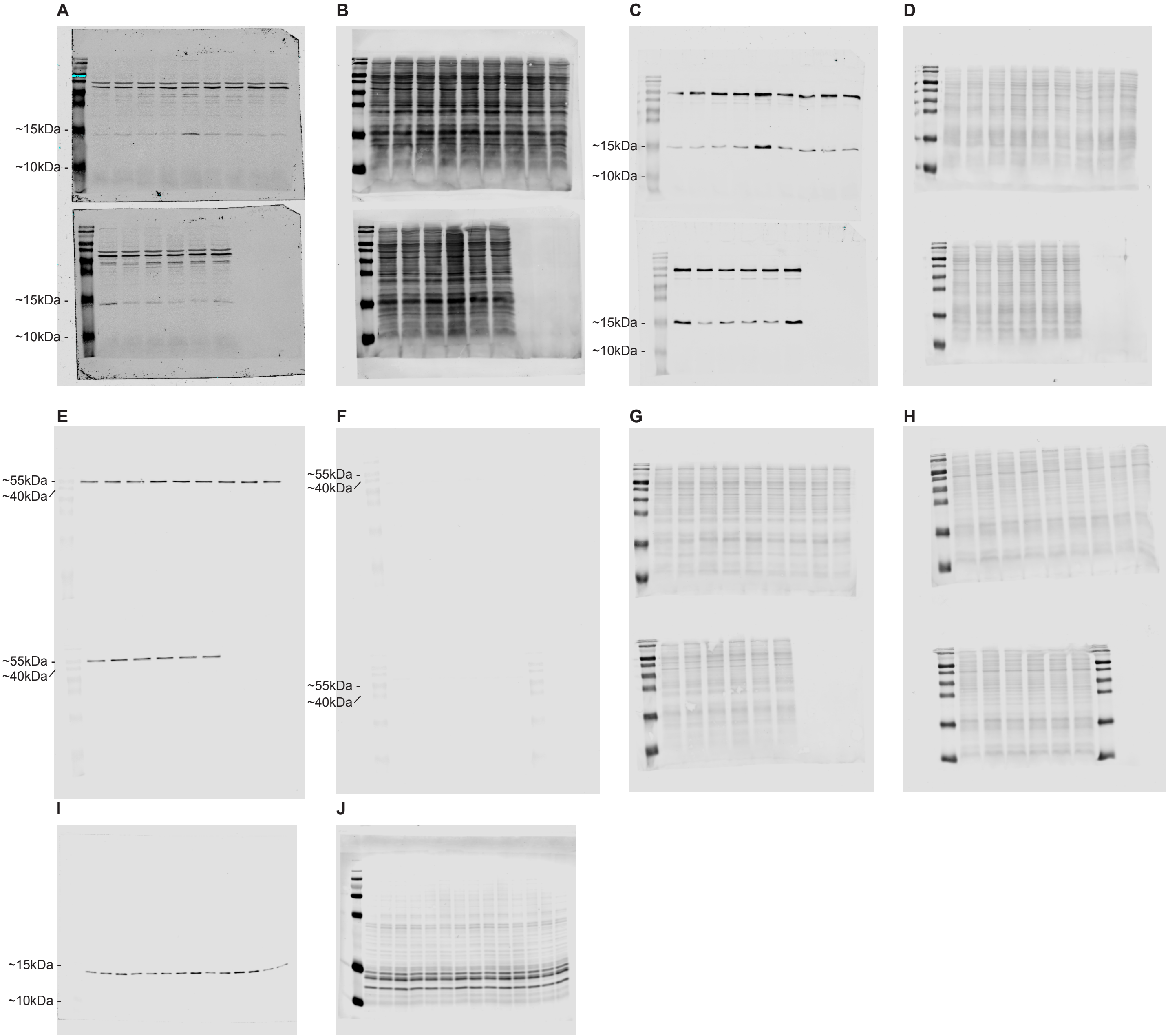


Figure S7: (*A-E*) Bar graphs illustrating log2 fold-changes for individual H3K4, H3K18/K23, H3K27, H3K36, and H4 PTMs in liver from Met-restricted C57BL/6J mice relative to age-matched controls as measured by LC-MS/MS. n≥5, error bars represent SD, *p<0.05 (Welch's t-Test) within PTM, #p<0.05 (Welch's t-Test) across PTMs. (*F*) Bar graph illustrating changes in fat, lean mass, and total body mass (BW) after 3 weeks of control or Met-restricted diet feeding. n=14, error bars represent SEM, *p<0.05 (two-way ANOVA). (*G*) Glucose tolerance test in 6- and 22-month C57BL/6J mice after 2 weeks of control or Met-restricted diet feeding. n=14, error bars represent SEM, *p<0.05 (two-way ANOVA). (*H*) Bar graph illustrating changes in fat, lean mass, and total body mass (BW) after 5 weeks of control diet feeding following either 3 weeks of control or Met-restricted diet feeding. n≥6, error bars represent SEM, *p<0.05 (two-way ANOVA). (*I*) Glucose tolerance test in 6- and 22-month C57BL/6J mice after 4 weeks of control diet feeding following either 3 weeks of control or Met-restricted diet feeding. n≥7, error bars represent SEM, *p<0.05 (two-way ANOVA). See also Table S1 and Table S2.

Data S1. Related to Figure 3 and S3.
Primary Antibody and REVERT Total Protein Stain Western Blot Membranes



Data S1. Related to Figure 3 and S3. Primary Antibody and REVERT Total Protein Stain Western Blot Membranes: (*A*) Cytoplasm anti-H3K9me1 (Figure 3E). (*B*) REVERT Total Protein Stain for cytoplasm anti-H3K9me1 (Figure 3E). (*C*) Cytoplasm anti-H3 (Figure 3E). (*D*) REVERT Total Protein Stain for cytoplasm anti-H3 (Figure 3E). (*E*) Cytoplasm anti-α Tubulin (Figure 3E). (*F*) REVERT Total Protein Stain for cytoplasm anti-αTubulin (Figure 3E). (*G*) Nucleoplasm anti-α Tubulin (Figure 3E). (*H*) REVERT Total Protein Stain for nucleoplasm anti-αTubulin (Figure 3E). (*I*) Purified histone anti-H3K9me1 (Figure S3F). (*J*) REVERT Total Protein Stain for purified histone anti-H3K9me1 (Figure S3F).