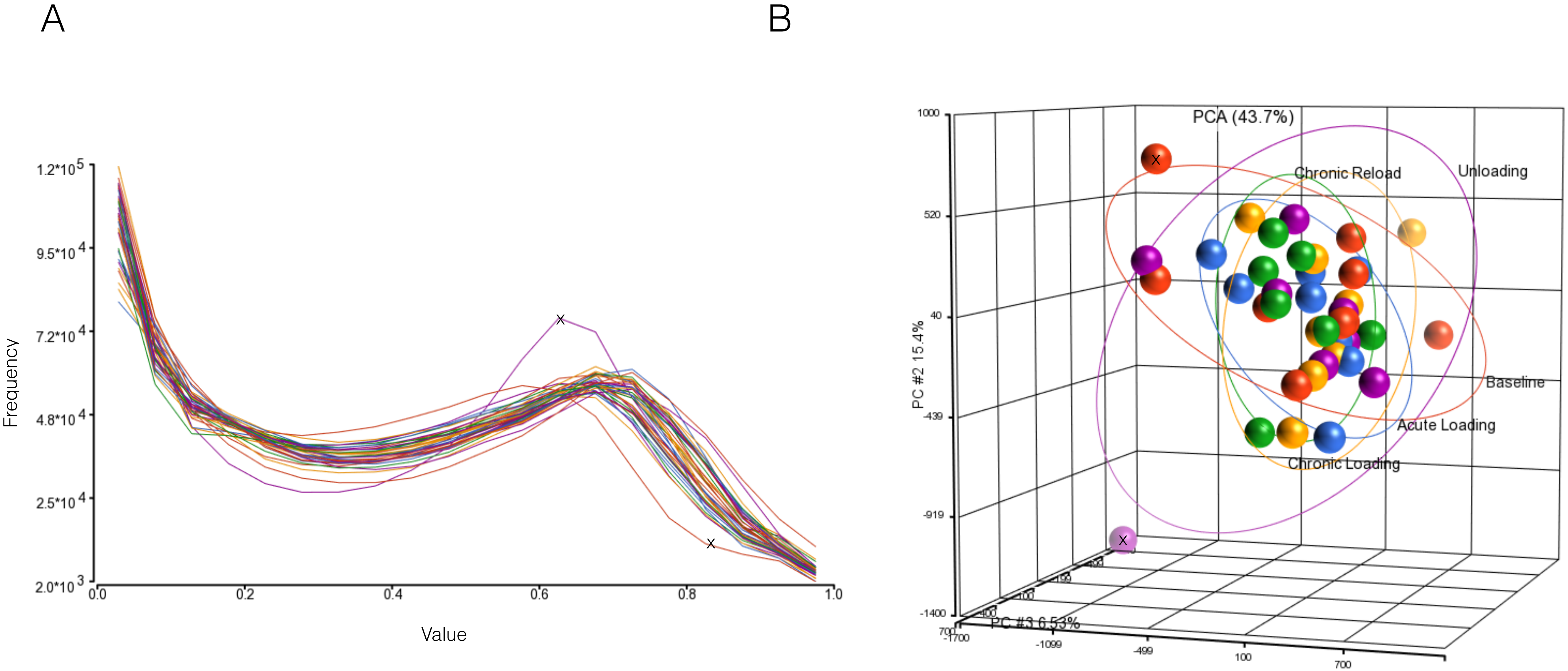

Supplementary Figure 1. Initial quality control analysis of human samples utilised for down-stream methylome wide bead arrays. **1a.** Histogram plot representing the distribution of intensity for each probe allowing for detection of aberrant samples. **1b.** Figure displaying the average methylation profile across all detected CpG loci allowing for analysis of variability using three-dimensional principal component analysis (PCA), where each sample is represented by a dot and ellipses for each condition. Two samples are identified as being outliers (X) from both quality control procedures and were subsequently removed from down-stream analysis.

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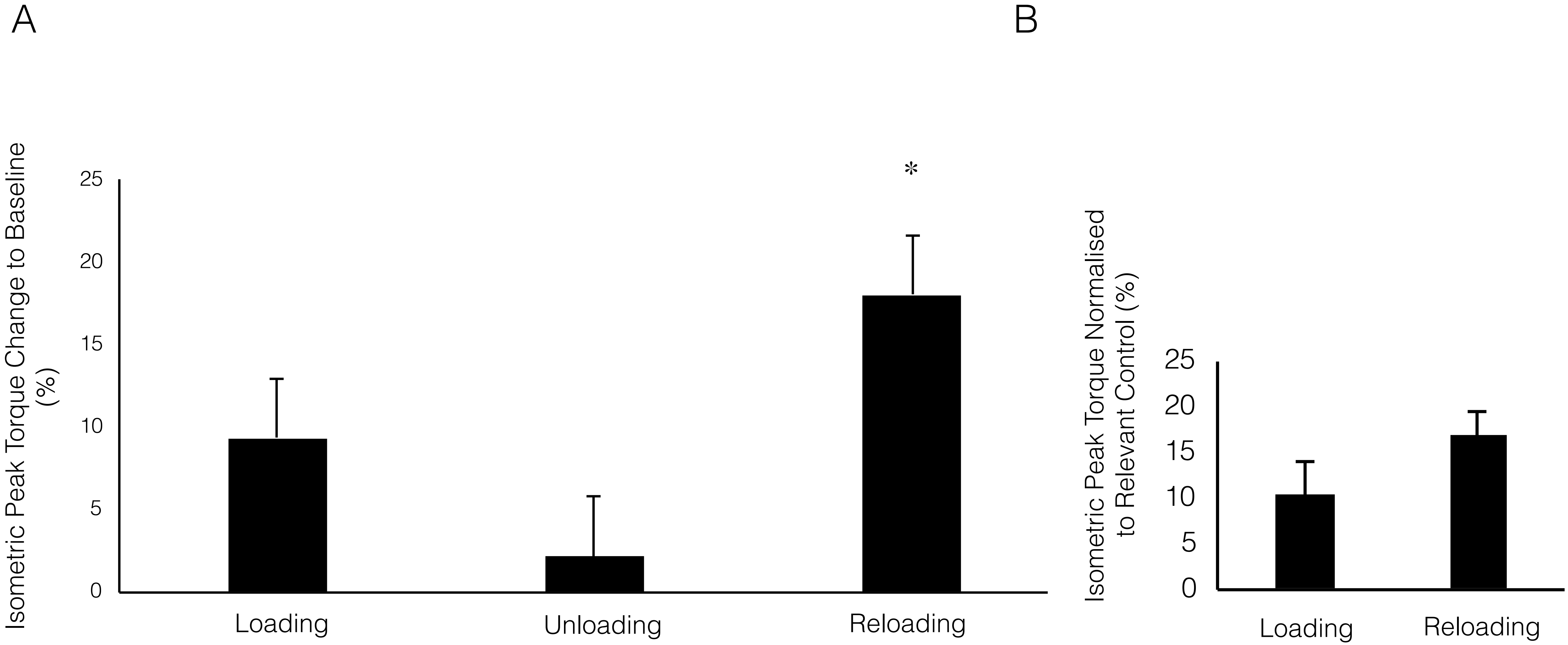

Supplementary Figure 2. Isometric quadriceps peak torque in human participants (n=7) after a period of 7 weeks' resistance exercise (loading), exercise cessation (unloading) and a subsequent second period of 7 weeks' resistance exercise (reloading) (Sup Fig 1a.). Significant change compared to baseline represented by *. **1b**. Isometric peak torque change when loading is normalised to baseline, and reloading normalised to unloading to account for any residual strength from the loading period. Pairwise t-test of significance indicated by *. All data presented as mean ± SEM (n=7).

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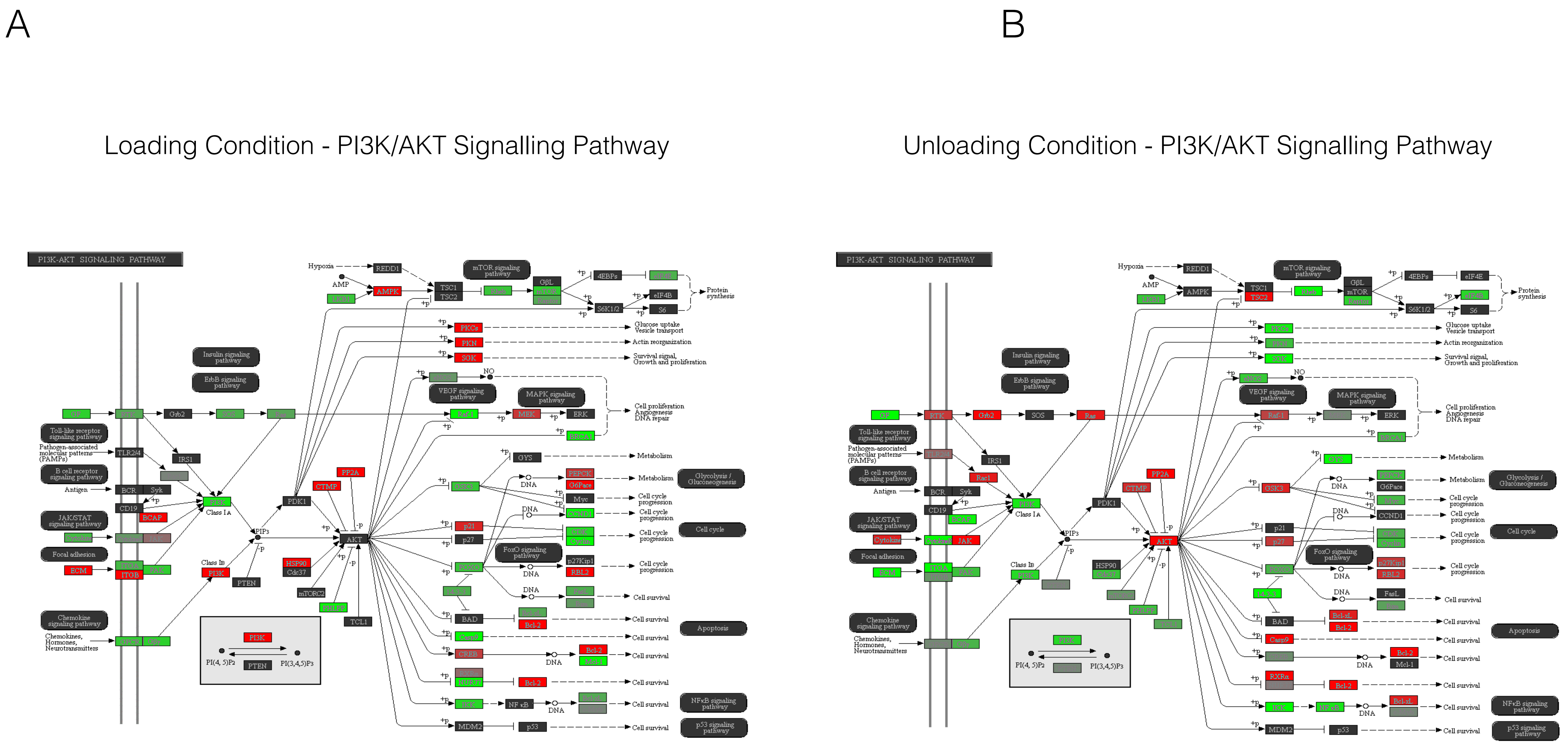

Supplementary Figure 3. Representation of the DNA methylation modifications that occurred within the PI3K/AKT signalling pathway following 7 weeks of loading (S**upp. figure 3a**) and unloading (S**upp. figure 3b**) in human subjects. Signalling analysis performed on statistically differentially regulated CpG sites compared to baseline, with green indicating a hypomethylated fold change and red indicating a hypermethylated change, with strength of colour representing the intensity of fold change [23-25].

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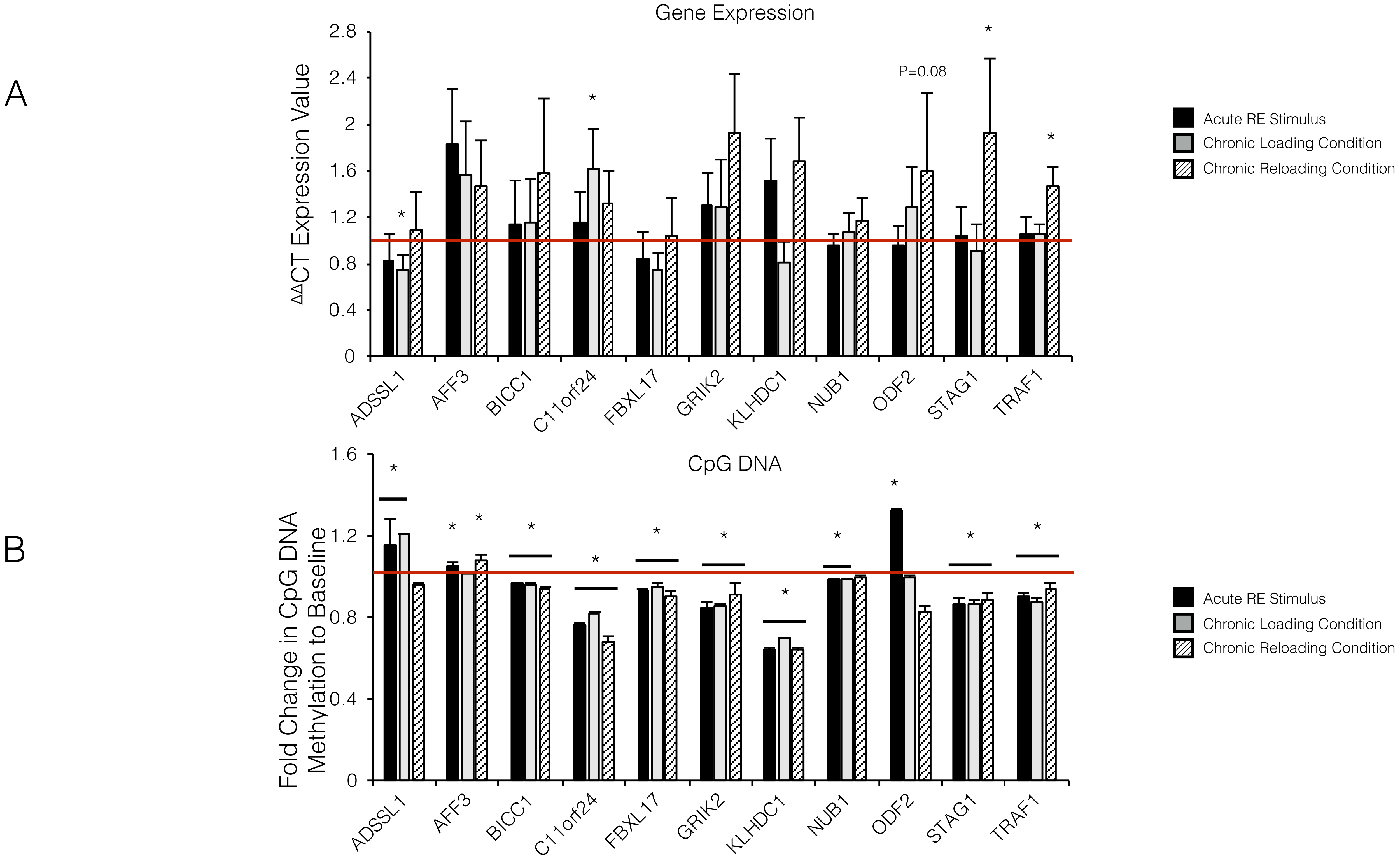

Supplementary Figure 4. Relative fold changes in; **a,** gene expression, and, **b,** CpG DNA methylation in all 18 gene transcripts identified from comparison of methylome data from acute RE vs. 7 weeks loading, unloading, reloading analysis. Data represented as means ± SEM, with significance compared to baseline (red line) indicated by *.

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