Supplementary figures and figure legends for:

Clobetasol promotes neuromuscular plasticity in mice after motoneuronal loss via sonic hedgehog signaling, immunomodulation and metabolic rebalancing

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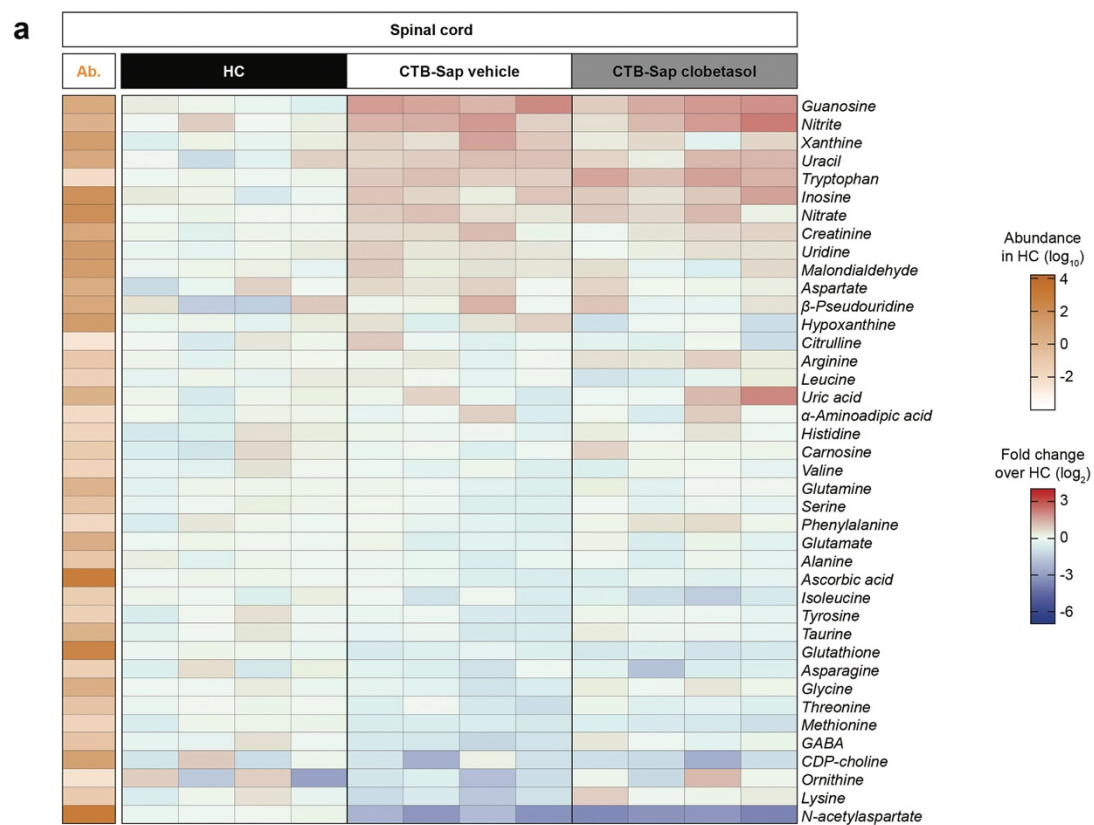

Fig. S1 I Clobetasol modifies metabolism of MN-depleted spinal cord. a, Heat maps of 40 metabolites in HC, CTB-Sap vehicle and CTB-Sap clobetasol spinal cord at 42 dpl showing the abundance (Ab.) in HC and the relative changes in CTB-Sap vehicle and CTB-Sap clobetasol as compared to HC; data are shown $\log_{10}$ abundance and $\log_2$ FC over HC of n = 4 mice per group.
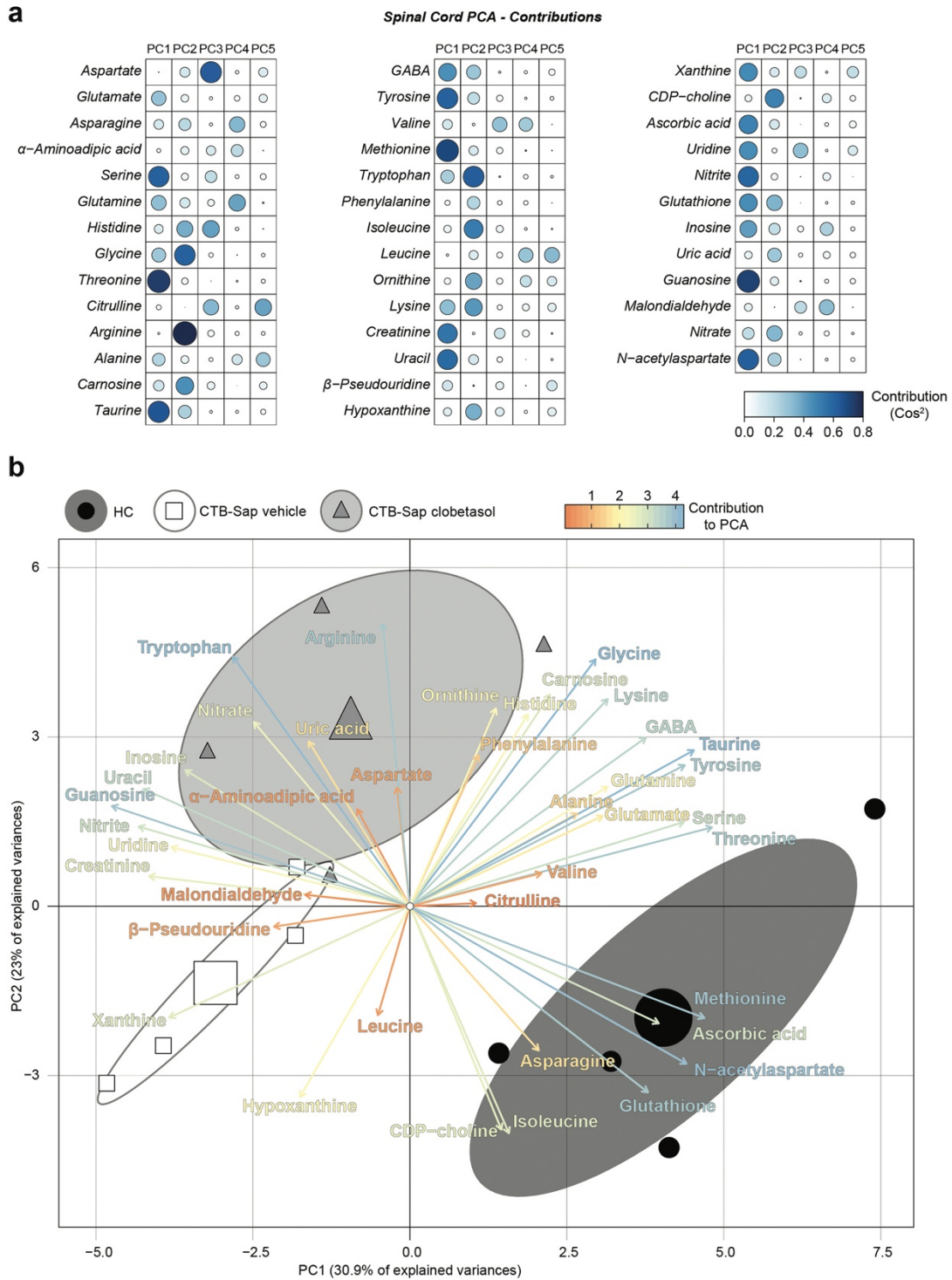
Fig. S2 l Principal components analysis (PCA) of spinal cord metabolites in HC, CTB-Sap vehicle and CTB-Sap clobetasol mice. a, Factor map of quality plot representation of the variables on PC1-PC5 expressed as square cosine (Cos^2). **b**, PCA biplot of 40 metabolites for HC, CTB-Sap vehicle and CTB-Sap clobetasol; key-colored arrows represent the contribution of each variable to the PCA; small circles/squares/triangles represent single subjects and large circles/squares/triangles represents the mean point of the confidence ellipses.
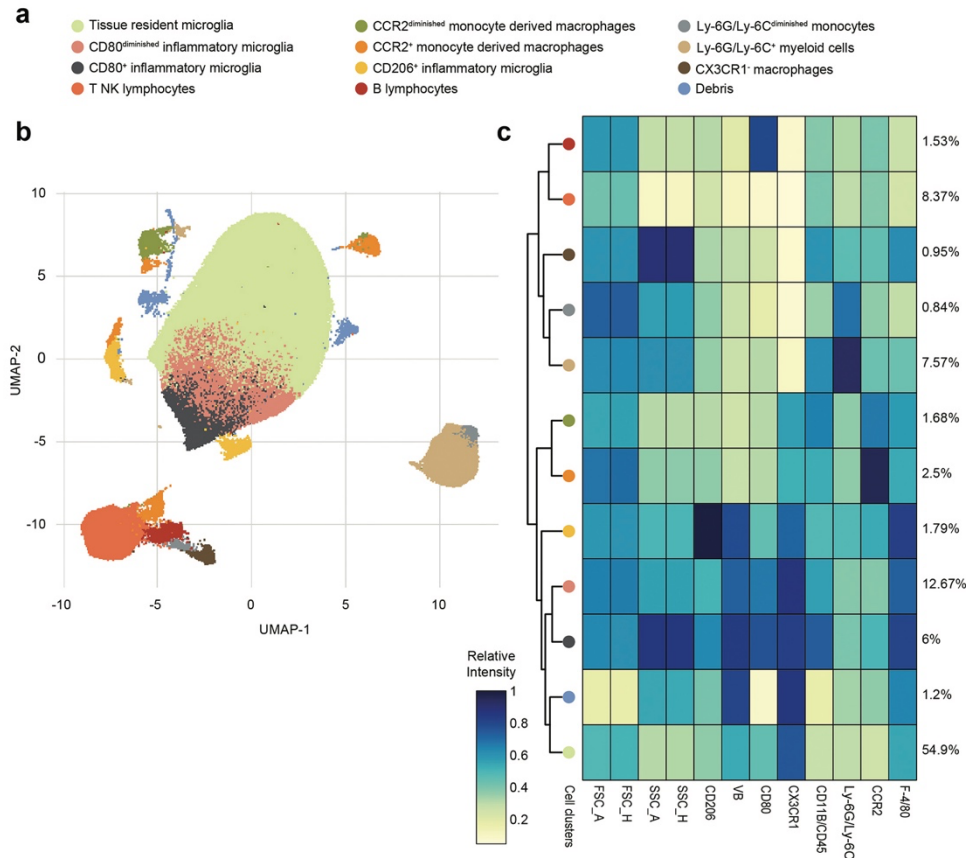
Fig. S3 I Cell populations identified by multi-step bioinformatics analysis of flow cytometry panel. a, b, Uniform Manifold Approximation and Projection (UMAP) representation of the populations identified through flow-cytometry by "fusing" all the events from the 12 samples (4 mice for 3 conditions).

c, Heatmap showing the expression of each marker in each population. The differential expression was used to assign, in a supervised manner, each cluster to each immune population. The overall abundance of each subpopulation is reported within the heatmap.
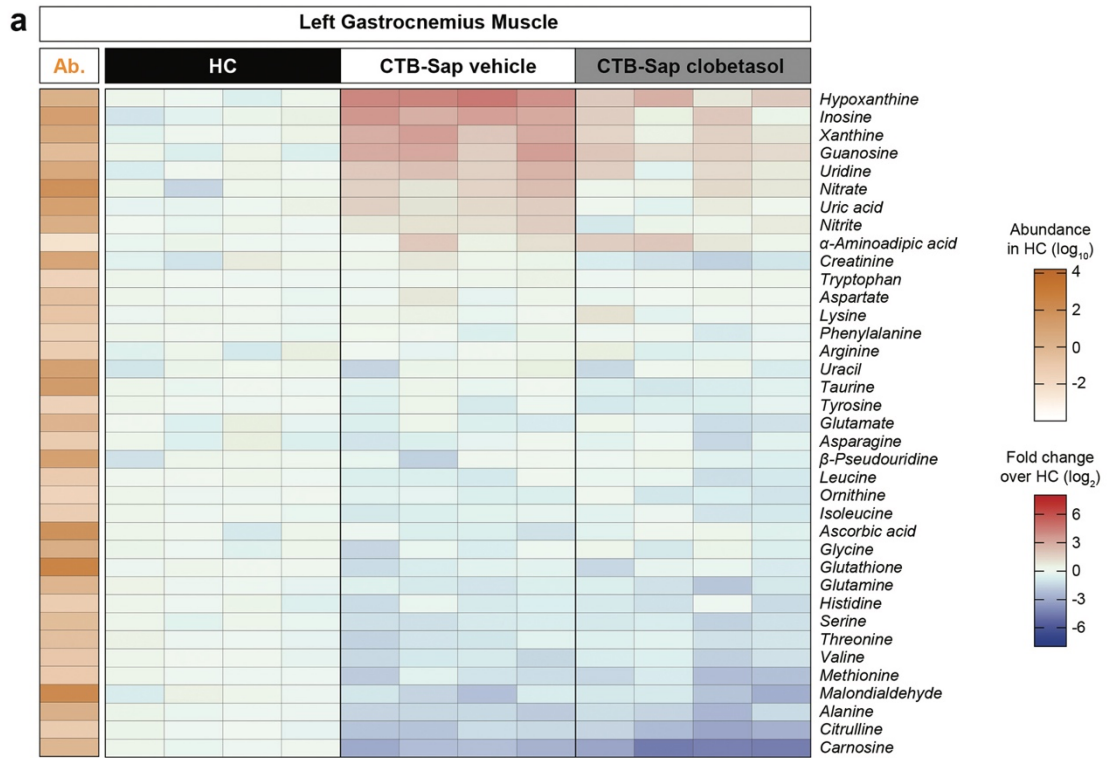
Fig. S4 l Effects of clobetasol onto contralateral, unaffected muscle. a, Heat maps of 37 metabolites in the right GM HC, CTB-Sap vehicle and CTB-Sap clobetasol at 42 dpl showing the abundance (Ab.) in HC and the relative changes in CTB-Sap vehicle and CTB-Sap clobetasol as compared to HC; data are shown as $\log_{10}$ abundance and $\log_2$ FC over HC of n = 4 mice per group.

b, Heat maps of 24 metabolites in the right GM HC, CTB-Sap vehicle and CTB-Sap clobetasol at 42 dpl showing the abundance (Ab.) in HC and the relative changes in CTB-Sap vehicle and CTB-Sap clobetasol as compared to HC; data are shown as $\log_{10}$ abundance and $\log_2$ FC over HC of n = 4 mice per group.

Fig. S5. Clobetasol modifies metabolism of denervated muscle. a, Heat maps of 37 metabolites in the left GM HC, CTB-Sap vehicle and CTB-Sap clobetasol at 42 dpl showing the abundance (Ab.) in HC and the relative changes in CTB-Sap vehicle and CTB-Sap clobetasol as compared to HC; data are shown as $\log_{10}$ abundance and $\log_2$ FC over HC of n = 4 mice per group.
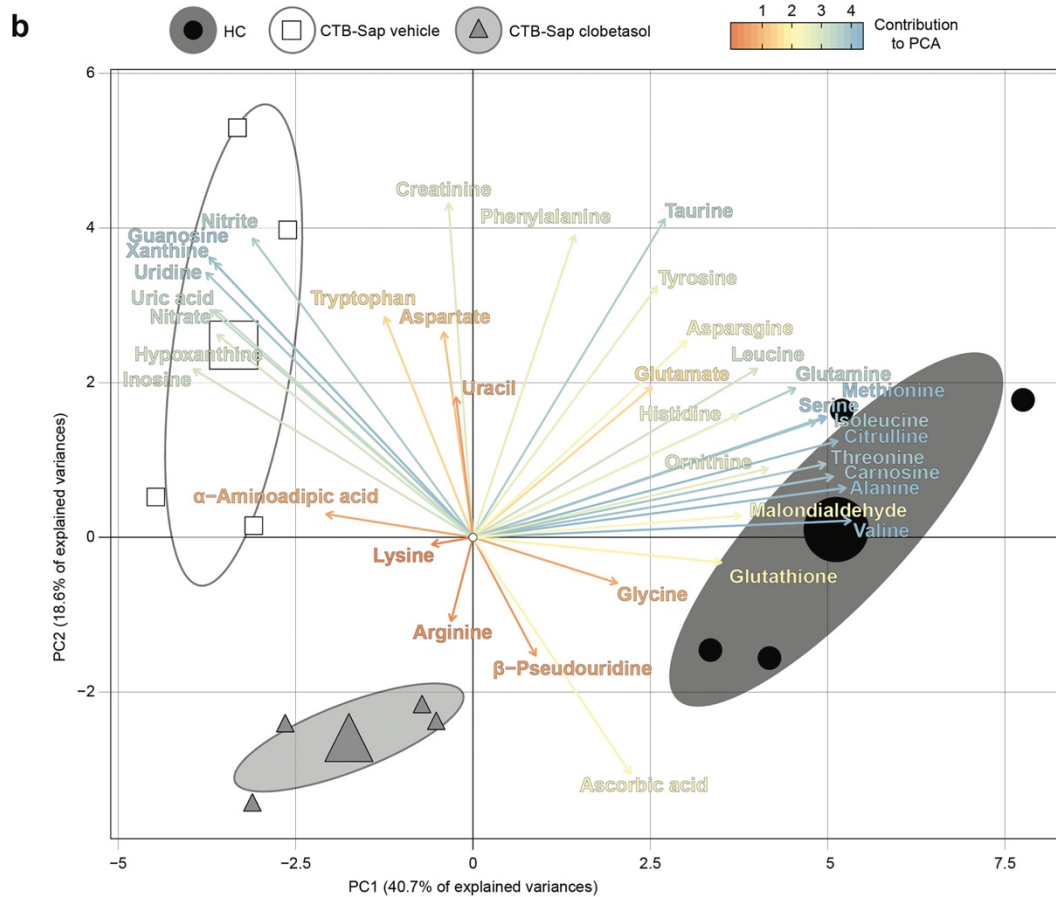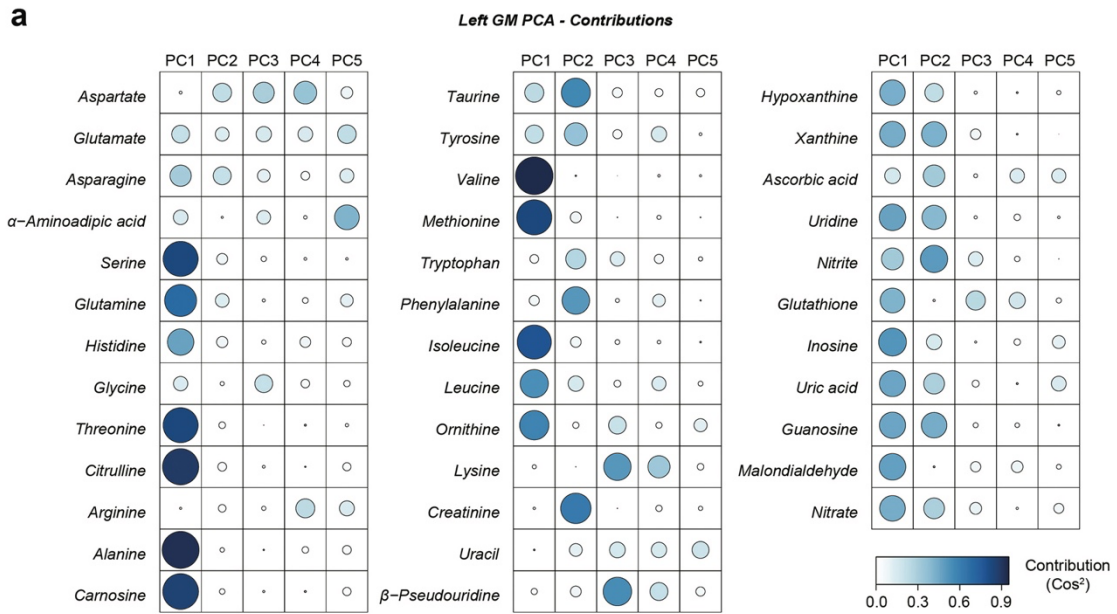
Fig. S6. Principal components analysis (PCA) of left GM metabolites of HC, CTB-Sap vehicle and CTB-Sap clobetasol mice. a, Factor map of quality plot representation of the variables on PC1-PC5 expressed as square cosine (Cos²). **b**, PCA biplot of 37 metabolites for HC, CTB-Sap vehicle and CTB-Sap clobetasol; key-colored arrows represent the contribution of each variable to the PCA; small circles/squares/triangles represent single subjects and large circles/squares/triangles represents the mean point of the confidence ellipses.
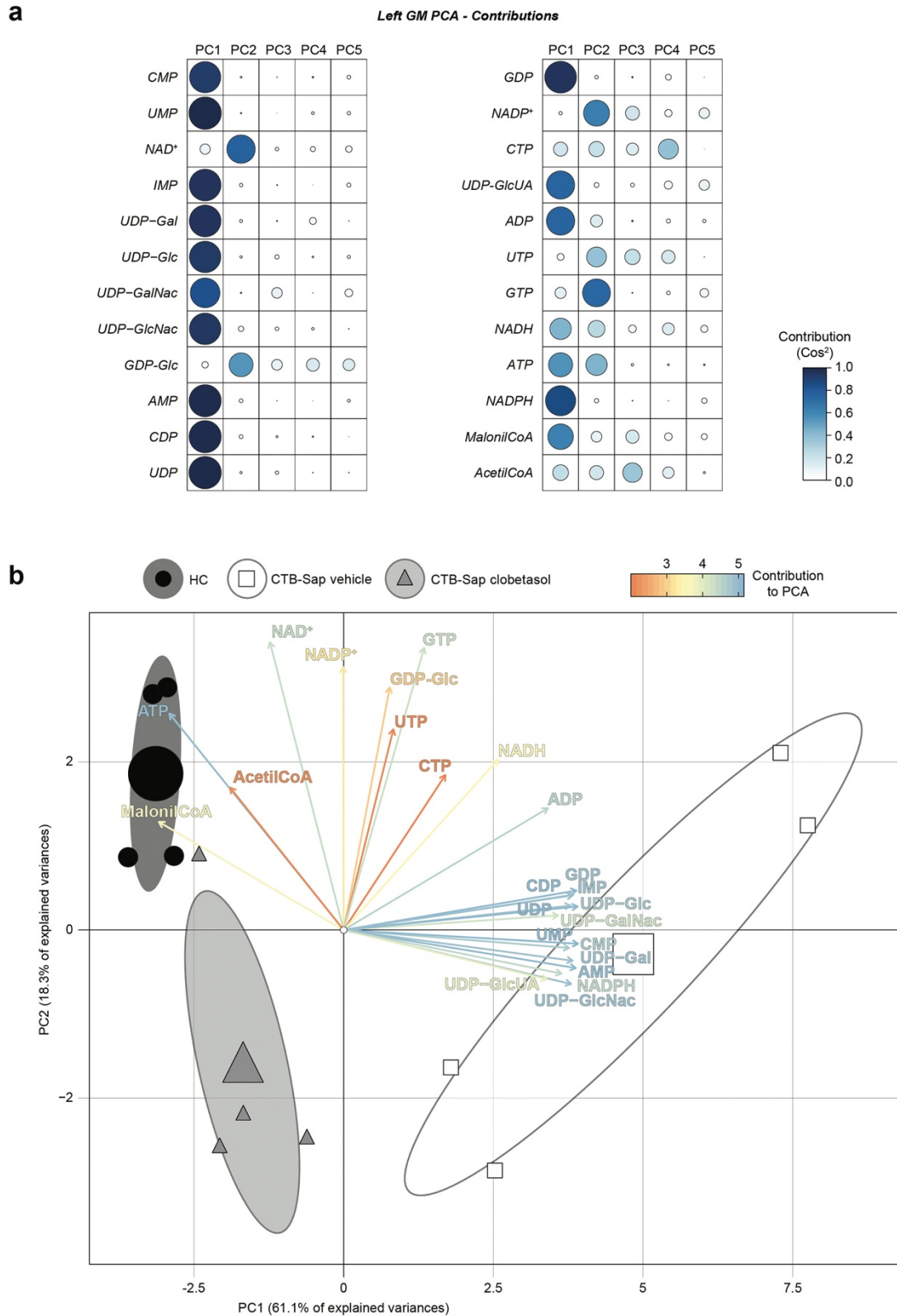
Fig. S7. Principal components analysis (PCA) of left GMs metabolites of HC, CTB-Sap vehicle and CTB-Sap clobetasol mice. a, Factor map of quality plot representation of the variables on PC1-PC5 expressed as square cosine (Cos^2). **b,** PCA biplot of 24 metabolites for HC, CTB-Sap vehicle and CTB-Sap clobetasol; key-colored arrows represent the contribution of each variable to the PCA; small circles/squares/triangles represent single subjects and large circles/squares/triangles represents the mean point of the confidence ellipses.