***Non-targeted metabolomics analysis.*** After HL-1 cells were cultured for 16 h in specialized 6well BioFlex® culture plates in Claycomb medium, medium was changed to DMEM supplemented 1% penicillin-streptomycin and 10% serum. Transient knockdown of MuRF1 was carried out using recombinant Ad.shRNA MuRF1 at MOI 30. After transduction for 48 h, HL-1 cells were used for mechanical stretch at 15% strain and for different times (15, 30, and 60 min) in a computer-regulated Flexcell® FX-5000™ Compression System (Flexcell International Corporation, Hillsborough, NC). Non-stretch cells (0 min) were used as the control. After HL-1 cells were stretched, HL-1 cells (at 0 and 60 min) and DMEM medium (at 0, 15, 30, and 60 min) were collected for GC/MS measurement of metabolites, and samples were placed on dry ice/stored at **-**80C. Samples were then analyzed by GC/MS, as previously described [24]. The raw, transformed, and sorted data used for each of the three comparisons in the metabolomics analyses can be found in **Supplemental Table 1**. Up to 1 missing value per group was imputed using lowest value in the same group, with groups missing 2 or more excluded from the analysis. The data obtained in this study will be accessible at the NIH Common Fund’s Data Repository and Coordinating Center (supported by NIH grant, U01-DK097430) website, [http://www.metabolomicsworkbench.org](http://www.metabolomicsworkbench.org/).

***Metabolomic Statistical Analyses.*** Metaboanalyst (v3.0) run on the statistical package R (v2.14.0) used metabolite peaks areas (as representative of concentration)19-21, as previously described [25]. These data were first analyzed by an unsupervised principal component analysis (PCA), which identified MuRF1 knockdown as the principal source of variance. A One-Way Analysis of Variance (ANOVA) across the eight groups at different time points was performed (Ad.shRNA Scr-0, Ad.shRNA MuRF1-0, Ad.shRNA Scr -15, Ad.shRNA MuRF1-15, Ad.shRNA Scr -30, Ad.shRNA MuRF1-30, Ad.shRNA Scr-60, Ad.shRNA MuRF1-60,) using Metaboanalyst v3.0. Metabolites identified and detected in all groups were included in the One-Way ANOVA. If two or more values of each metabolite were missing in a given group, the entire metabolite was removed from the analysis. Data used in this study are available in **Supplemental Table 1**. Heat maps were generated using the GENE- E software

(http://www.broadinstitute.org/cancer/software/GENE-E/index.html). All data is shown as mean +/- SEM, unless otherwise indicated.