



### Supplementary Figure S6.

Total levels of cysteine and glutathione intermediates in lung cancer models (related to Fig. 5). **A**, Analysis of the total signal of serine, glycine, cystathionine, glutathione, cysteine and  $\gamma$ -glutamylcysteine in normal lung tissues (N=8) compared to Nrf2<sup>WT</sup> lung adenocarcinoma (LUAD) and (N=10), Nrf2<sup>D29H</sup> LUAD tumors (N=10) and their matched serum from normal (N=8), Nrf2<sup>WT</sup> (N=5), and Nrf2<sup>D29H</sup> (N=5) following infusion with 1-[<sup>13</sup>C<sub>3</sub>]-serine. **B**, Analysis of the total signal of serine, glycine, cystathionine, glutathione, cysteine and  $\gamma$ -glutamylcysteine in normal lung tissues (N=8) compared to small cell lung cancer (SCLC) tumors (N=9), and their matched serum normal (N=8) and SCLC (N=9) following infusion with 1-[<sup>13</sup>C<sub>3</sub>]-serine. N.B. the control lung samples in **A** are the same as in **B**. Data are presented as mean  $\pm$  SD. N.D., not detected. The total signal is the sum of all isotopologue signals. The peak intensities of isotopologues were measured as AreaTop (mean of three top points in the peak). Ser, serine; Cth, cystathionine; Cys, cysteine; Gly, glycine; GSH, glutathione;  $\gamma$ -Glu-Cys,  $\gamma$ -glutamylcysteine. \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, and \*\*\*\*p < 0.0001. **C**, Log scaled gene expression profile for CBS and CSE in LUAD (lung adenocarcinoma) and LUSC (lung squamous cell carcinoma) datasets in TCGA and GTEx. |Log<sub>2</sub>FC| cutoff, 1; p-value cutoff, 0.01; log-scale, log<sub>2</sub>(TPM+1).