

## **Description of Additional Supplementary Files**

File Name: **Supplementary Data 1**

Description: List of 12,653 peptide transition groups available for monitoring 3593 unique proteotypic SH peptides of 215 SHs, related to Supplementary Fig. 1

(A manually compiled total reference list of 335 SHs in the source data.)

File Name: **Supplementary Data 2**

Description: Reference set of internal standard peptides (ISPs) related to Supplementary Fig. 2

File Name: **Supplementary Data 3**

Patient Information

File Name: **Supplementary Data 4**

Description: List of 131 SHs measured in the LUAD study and their corresponding 793 proteotypic peptides (916 peptide transitions) identified by SWATH-MS at peptide FDR <0.001, related to Figure 3.

File Name: **Supplementary Data 5**

Description: List of 2078 Proteins - 1<sup>st</sup> degree interactors of 72 SH (RADDi, KS<=0.05), related to Figure 5

File Name: **Supplementary Data 6**

Description: List of 978 Proteins co-depleted with the active SHs. 933 out of 978 proteins are annotated as 1<sup>st</sup> or 2<sup>nd</sup> degree interactors in Integrated Interactions Database.

File Name: **Supplementary Data 7**

Description: The binary enzyme:protein interactions across co-depleted proteome based on canonical correlation analysis (CCA) via DIABOLO data integration tool, related to Figure 5.

File Name: **Supplementary Data 8**

Description: Profiling of FA levels in patient tumor lysates, related to Figure 6.

File Name: **Supplementary Data 9**

Description: Original output values of respective metals (Conc. [ng/ml], Conc. RSD and intensity (CPS), related to Figure 7.