Electronic Supplementary Material (ESI) for Molecular BioSystems.

Dataset S1: Median normalised SILAC ratios of COLA fractionation mixes. Log2 of SILAC ratios from two replicate experiments with reciprocal labelling (Fraction H/ lysate L and Fraction L/ lysate H) for proteins with valid ratios in all experiments are displayed. Ratio H/L count: The number of SILAC quantification ratios for each protein; Protein IDs: Uniprot accessions for all matching proteins; Majority protein IDs: Uniprot accessions for the major entries; Protein names: Uniprot exhaustive proteins names; Gene names: Uniprot coding gene names;

Dataset S2: 2-Dimensional annotation enrichment analysis of GOCC categories in subcellular fractions. SILAC ratios from the two reciprocal experiments were subjected to 2D annotation enrichment enrichment analysis as described in[21]. A Benjamini-Hochberg FDR rate of 0.02, and a delta score (enrichment score) of 0.2 was used as cut-off. Delta scores show the level of enrichment in each replicate (positive for enriched and negative for depleted) while p-value and FDR columns show the significance of a calculated enrichment. Variable columns show the name of the fractions as defined in Dataset S2, on which the two dimensional enrichment was performed. Fraction numbers are as displayed in Fig. 1B. Category size shows the number of proteins in each category that were present in the dataset.

Dataset S3: List of all analysed proteins and their bootstrap cluster numbers at each p-value cut-off. Each cluster is designated by a number, displayed under bootstrapped clusters columns at each cut off p-value. 0 indicates that the protein was not found in a significant cluster at the given p-value. Gene number: The number describing the original place of a gene in the gene list of Dataset S1; Majority protein IDs: Uniprot accessions for the major entries; Protein names: Uniprot exhaustive proteins names; Gene names: Uniprot coding gene names;

Dataset S4: List of all binary protein-protein interactions derived from bootstrapped clusters (Dataset S3). The numbers 0 and 1 show at which bootstrapping cut off the interaction was reported (1: reported, 0: not reported). Whether the binary interaction was also found in any of the investigated reference databases (CORUM, STRING, and Pathway Commons) is similarly shown.

Dataset S5: Normalised reported ion intensity ratios (fraction/lysate) of TMT labelled fractionation mixes of A375P cells. F1 to F9 values are z-scored log2 of fraction to lysate ratios corresponding to subcellular fractions 1 to 9, as shown in Fig. 3A. Each value is averaged from 4 technical replicate injections. Proteins with valid ratios in all fractions are displayed. Protein IDs: Uniprot accessions for all matching proteins; Majority protein IDs: Uniprot accessions for the major entries; Protein names: Uniprot exhaustive proteins names; Gene names: Uniprot coding gene names;

Dataset S6: List of all analysed A375P proteins and their bootstrap cluster numbers at p-value cut-off of 0.05. Each cluster is designated by a number. Each cluster is designated by a number. 0 indicates that the protein was not found in a significant cluster at the given p-value. Majority protein IDs: Uniprot accessions for the major entries; Protein names: Uniprot exhaustive proteins names; Gene names: Uniprot coding gene names;

Dataset S7: List of A375P binary protein-protein interactions derived from bootstrapped clusters (Dataset S6), Whether the binary interaction was found in any of the investigated reference databases (CORUM, STRING, and Pathway Commons) is displayed in front of every interaction (1: reported, 0: not reported).

Dataset S8: Normalised reported ion intensity ratios (fraction/lysate) of TMT labelled fractionation mixes of A375M2 cells. F1 to F9 values are z-scored log2 of fraction to lysate ratios corresponding to subcellular fractions 1 to 9, as shown in Fig. 3A. Each value is

averaged from 4 technical replicate injections. Proteins with valid ratios in all fractions are displayed. Protein IDs: Uniprot accessions for all matching proteins; Majority protein IDs: Uniprot accessions for the major entries; Protein names: Uniprot exhaustive proteins names; Gene names: Uniprot coding gene names;

Dataset S9: List of all analysed A375M2 proteins and their bootstrap cluster numbers at p-value cut-off of 0.05. Each cluster is designated by a number. 0 indicates that the protein was not found in a significant cluster at the given p-value. Majority protein IDs: Uniprot accessions for the major entries; Protein names: Uniprot exhaustive proteins names; Gene names: Uniprot coding gene names;

Dataset S10: List of A375M2 binary protein-protein interactions derived from bootstrapped clusters (Dataset S9). Whether the binary interaction was found in any of the investigated reference databases (CORUM, STRING, and Pathway Commons) is displayed in front of every interaction (1: reported, 0: not reported).

Dataset S11: 1-Dimensional annotation enrichment analysis for the degree of interactome change amongst different identified protein categories in A375P and A375M2 iCOLA experiments. Ratio of the number of conserved (seen in both A375P and A375M2) / non-conserved (seen only in A375P or A375M2) interactions for each protein was calculated. The ratio values were then used in a 1D annotation enrichment analysis using GO, GSEA, CORUM, Pfam, SMART, KEGG, and Uniprot Keyword protein category databases [21], to reveal categories significantly enriched in conserved or non-conserved interactions. A Benjamini-Hochberg FDR rate of 0.02 was used as a significance cut-off for the enrichment analysis. Enrichment scores show the level of enrichment, with a positive value indicating enrichment in proteins with more conserved interactions, while a negative value indicates enrichment in proteins with more rewired interactions. The p-value and FDR columns show

the significance of a calculated enrichment. Category size shows the number of proteins in each category that were present in the dataset.