

**Table S4. Overview Perseus analysis of SILAC 2-4 proteome data**

<b>Matrix #</b>	<b>Processing</b>	<b>Description</b>
Matrix 1	Generic matrix upload	Load MaxQuant derived proteomics data from the tab-separated file proteinGroups.txt
Matrix 2-4	Filter rows based on categorical column	Remove proteins only identified by site Remove hits that match against a reverse nonsense database Remove potential contaminants
Matrix 5	Remove empty columns	Remove empty columns
Matrix 6	Select rows manually	Manual removal of immunoglobulin contaminants
Matrix 7	Transform	Inverse ratios (1/x)
Matrix 8	Matching rows by name	Combine columns of the existing protein ratios (Matrix 6) with the newly generated inverted ratios (Matrix 7)
Matrix 9	Transform	Log transformation of expression columns ( $\log_2(x)$ )
Matrix 10	Categorical annotation rows	Define columns with protein ratios as own group
Matrix 11	Reorder/remove columns	Selection of ratio columns of interest
Matrix 12-13	Categorical annotation row	Define protein ratios of biological replicates as a group
Matrix 14	Filter rows based on valid values	Filter protein ratios to be $\geq 0.5$ for two of three replicates (add categorical row)
Matrix 15	Filter rows based on valid values	Filter protein ratios to be $\geq 0.5$ for all three replicates (add categorical row)
Matrix 16	One-sample test	Right-sided one-sample t-test using a threshold p-value of 0.05
Matrix 17	One-sample test	Right-sided one-sample t-test using a threshold p-value of 0.01
Matrix 18	Rename columns	Give expression columns a more explicit name
Matrix 19	Fill categorical columns	Fill empty field in categorical columns with '-' to allow for later combining of categorical columns
Matrix 20-22	Combine categorical columns	Combine categorical columns of fold change filter and t-test
Matrix 23-26	Categorical annotation row	Define protein ratios of label-switch experiments as a group ('forward' & 'reverse' reaction)
Matrix 27-31	Average groups	Calculate mean of each group
Matrix 32	Filter rows based on valid values	Filter protein ratios to be $\geq 0.5$ for two of three replicates and reduce matrix for scatter plot generation