

Figure S6 Candidate assessment from SMC2 WT/EQ and SMC2 WT/Luc TAILS comparisons after removal of auto-cleavage sites. Detailed breakdown of candidates from volcano plots shown in Figure 4B to illustrate the 210 high confidence substrate cleavage sites and remaining unqualified regulated peptides. Panel from Figure 5C is included to show the distribution of SMC2 regulated peptides. A majority of WT/EQ regulated peptides met all the criteria for high confidence substrate cleavage sites, while roughly half of the WT/Luc regulated peptides were categorized as high confidence. In the case of the SMC2 TAILS dataset, the WT/EQ only average logFC was 1.0 versus the WT/EQ high confidence average of logFC of 2.5. While a predominance of high confidence hits were present in the WT/EQ regulated peptides, the WT/Luc regulated peptides contained a mixture of overlap with the activity associated WT/EQ comparison and the EQ/Luc regulated peptides likely associated with artifact from ADAMTS7 overexpression. For simplicity numbers reflect unique substrate cleavage sites, however the volcano plots contain all regulated peptides including multiple identifications for ADAM9_69 and COL1A2_113 within the SMC2 TAILS dataset.