

Figure S1. Schematic diagram of collection. 3D-printed integrated adapter collected the fractions from the qEV separation columns.

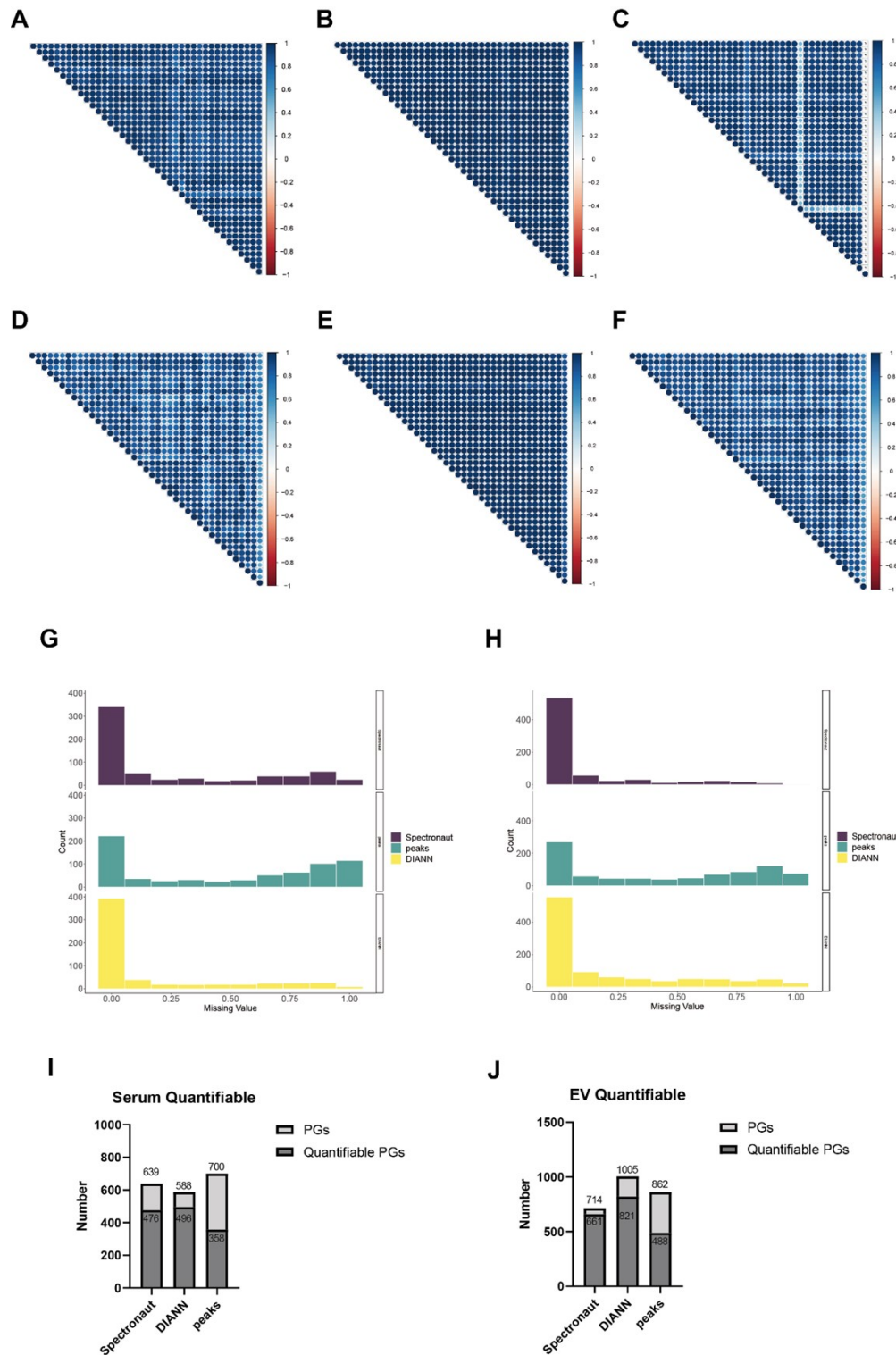


Figure S2. Software suites performance assessment in analyzing serum and serum EV proteomic data. (A-C) The correlation of 39 serum samples from Spectronaut, peaks and DIANN (left to right); (D-F) The correlation of 39 serum EV samples from Spectronaut, peaks and DIANN (left to right); (G) The Missing value distribution of 39 serum samples from Spectronaut, peaks and DIANN (left to right); (H) The Missing value distribution of 39 serum EV samples from Spectronaut, peaks and DIANN (left to right); (I and J) Performance of proteome identification and quantification in three software.

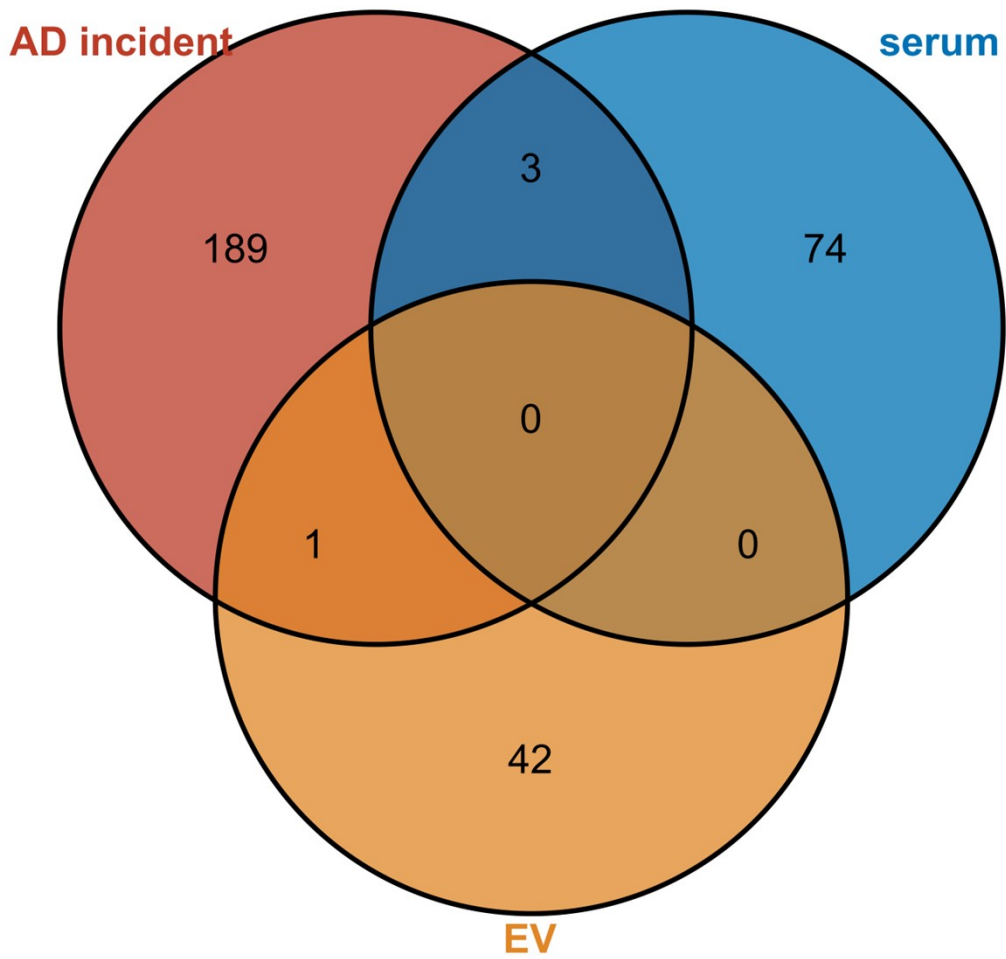


Figure S3. External data comparison. (A) Comparison between differentially expressed protein groups in Figure3 and external data.

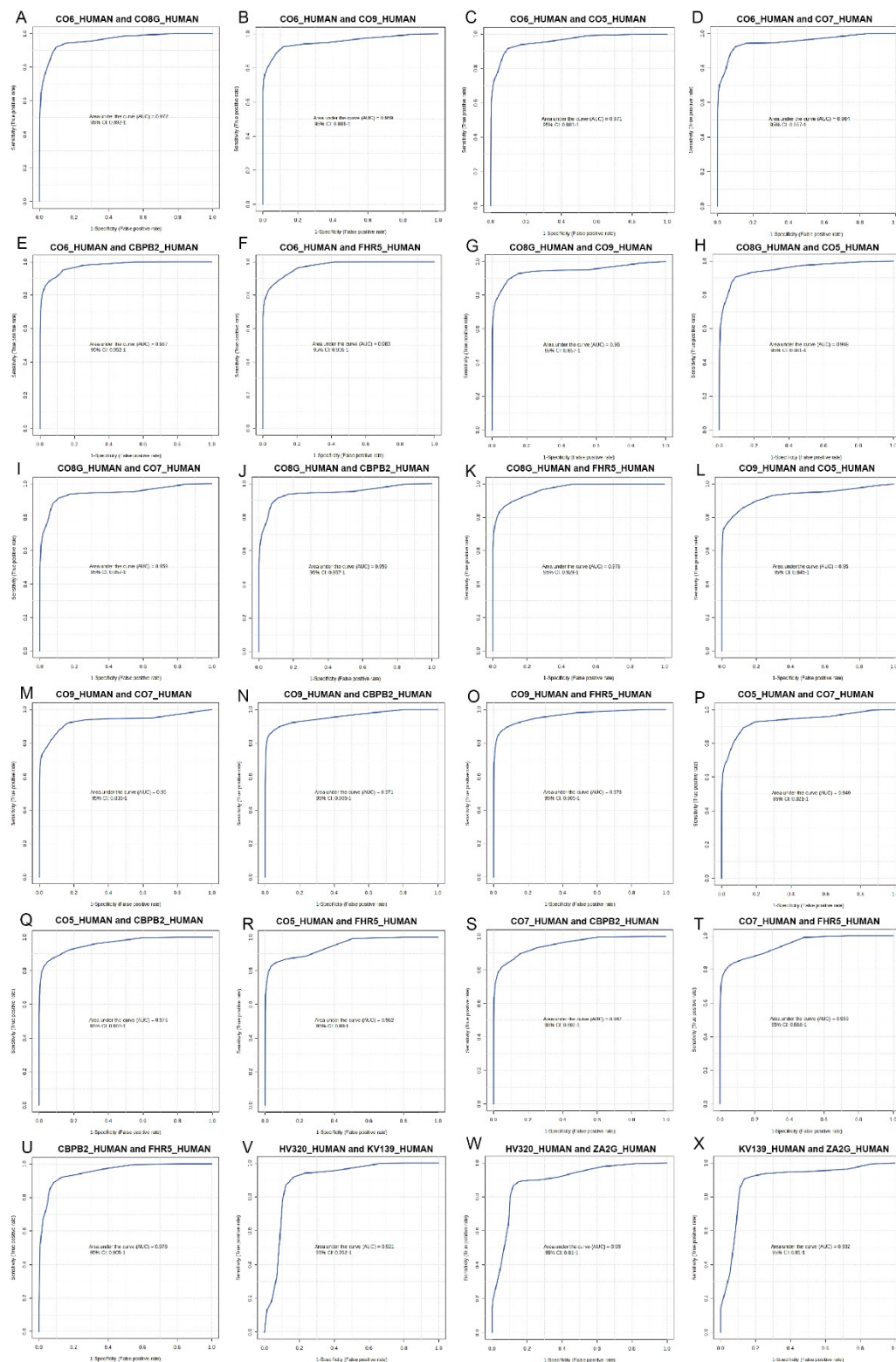


Figure S4. Diagnostic effect of the pairwise combination using top ten molecules. (A-U) Diagnostic effect of the pairwise combination using top seven molecules from serum EV. **(V-X)** Diagnostic effect of the pairwise combination using top three molecules from serum.