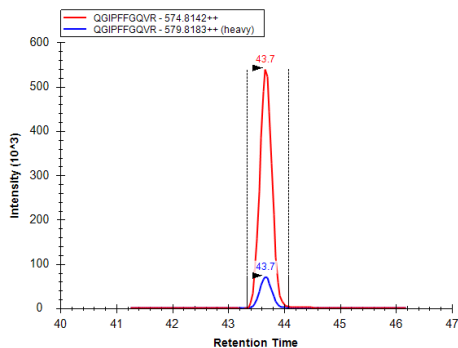
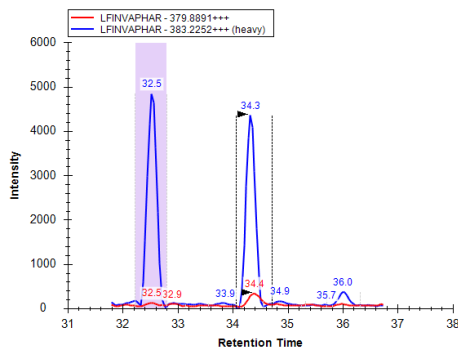


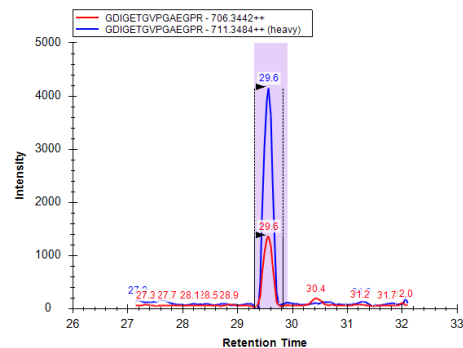
A2M, L/H = 7.476



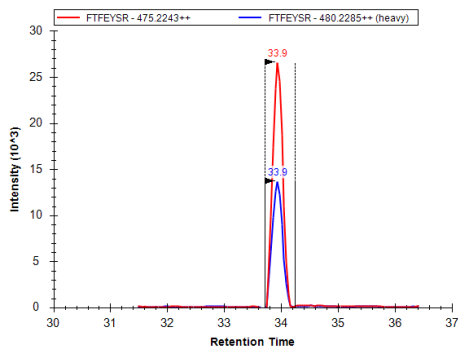
ADAMTS13, L/H = 0.091



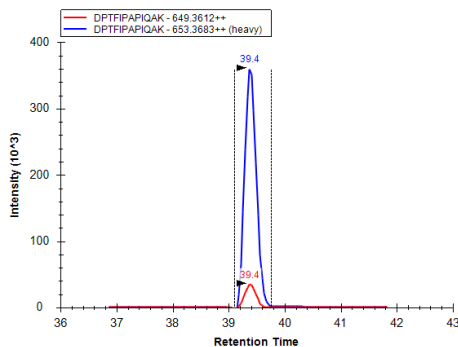
ADIPOQ, L/H = 0.328



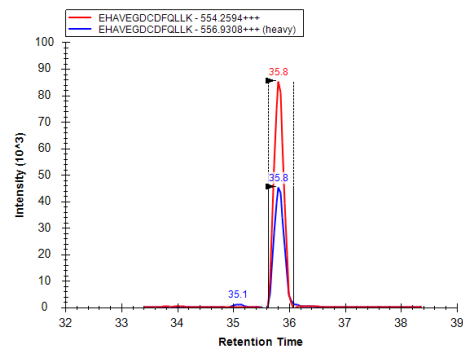
AFM, L/H = 1.891



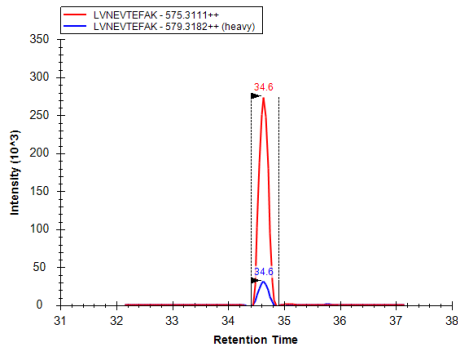
AGT, L/H = 0.093



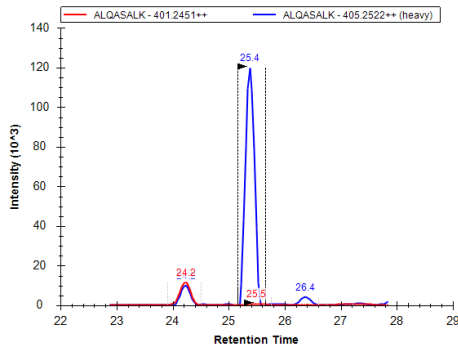
AHSG, L/H = 1.812



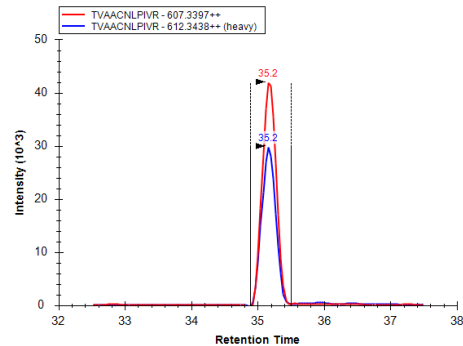
ALB, L/H = 8.503



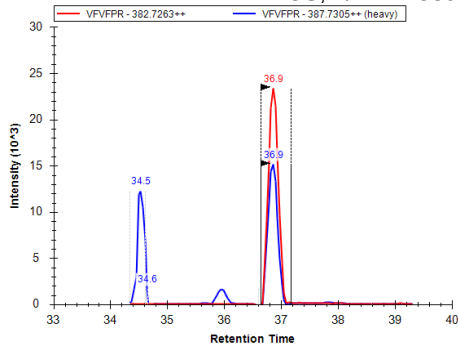
ALDOA, L/H = 0.009



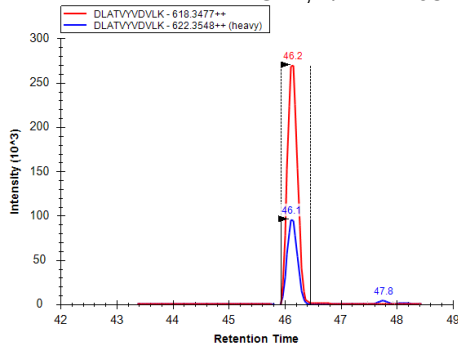
AMBP, L/H = 1.447



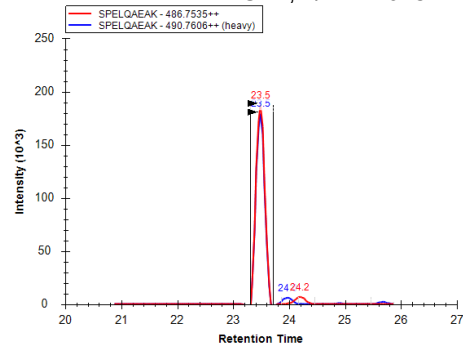
APCS, L/H = 1.589



APOA1, L/H = 2.798

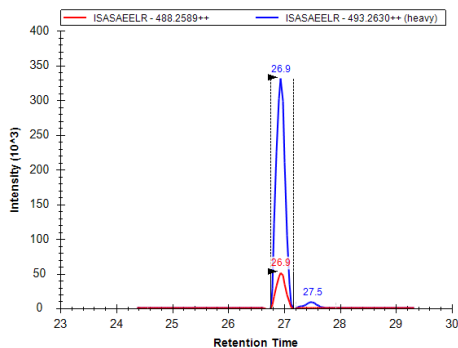


APOA2, L/H = 1.045

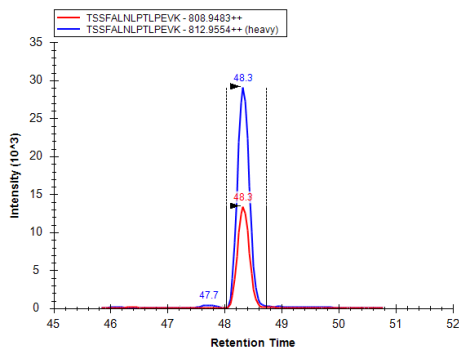


Supplementary Figure S1. Extracted Ion Chromatograms (XIC) of examples of light-to-heavy peptide peak area ratios of 119 proteins. Light-to-heavy peak area ratio values are shown in the upper right of the chromatograms. The chromatograms of light peptides are red, whereas chromatograms of the corresponding heavy peptides are blue.

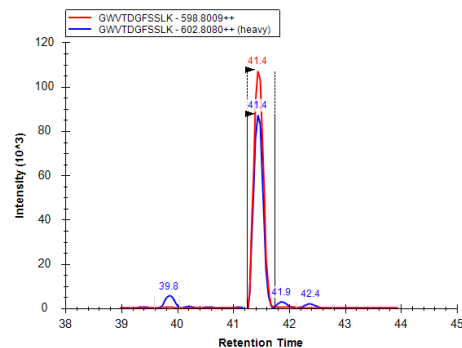
APOA4, L/H = 0.159



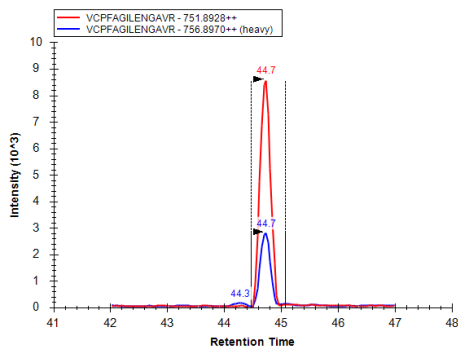
APOB, L/H = 0.451



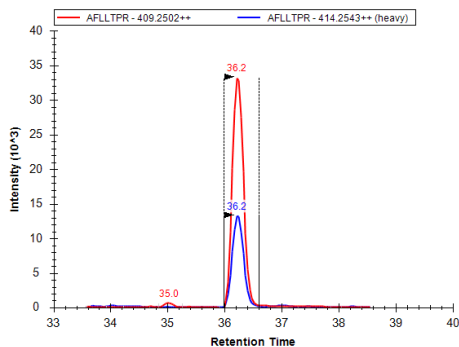
APOC3, L/H = 1.270



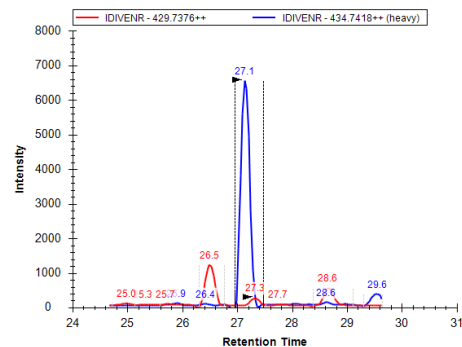
APOH, L/H = 3.218



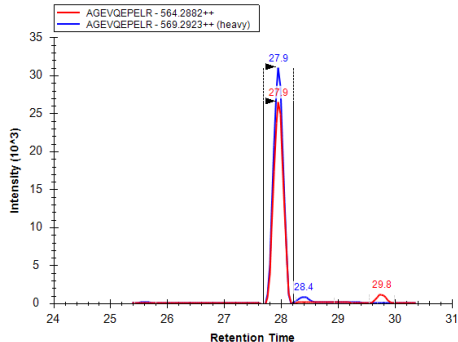
APOM, L/H = 2.478



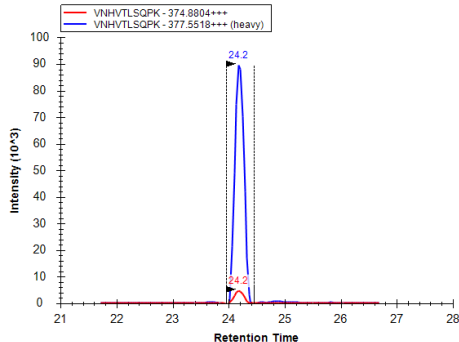
ASS1, L/H = 0.035



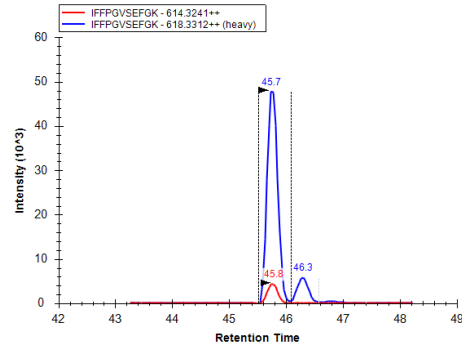
AZGP1, L/H = 0.859



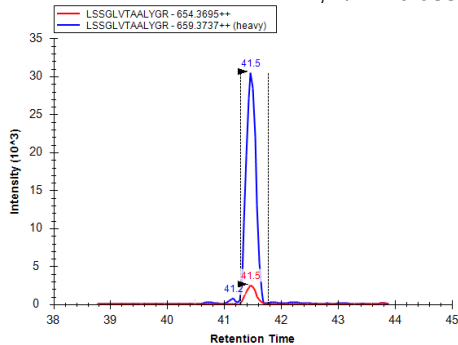
B2M, L/H = 0.053



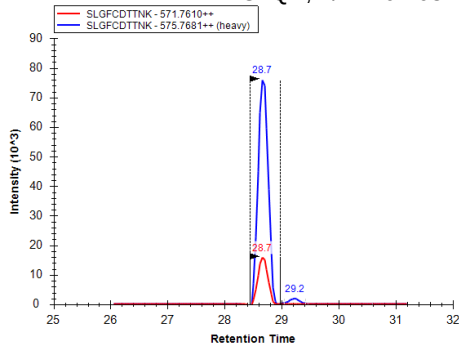
BCHE, L/H = 0.089



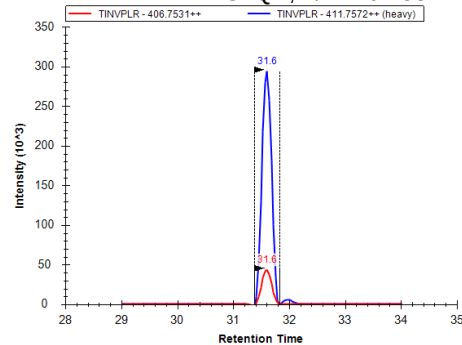
BTD, L/H = 0.083



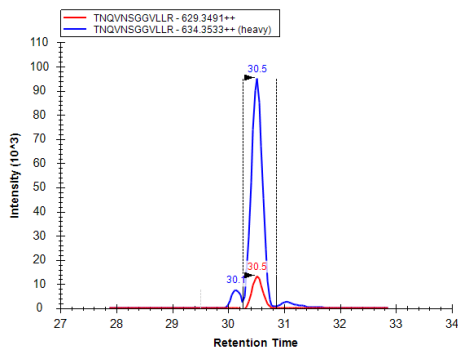
C1QA, L/H = 0.205



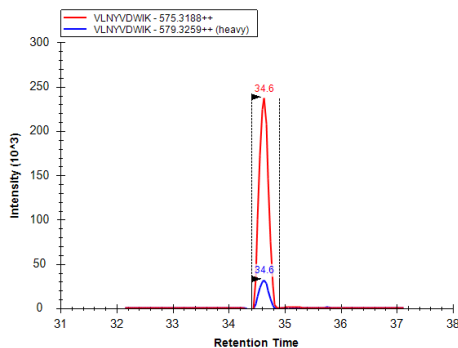
C1QB, L/H = 0.153



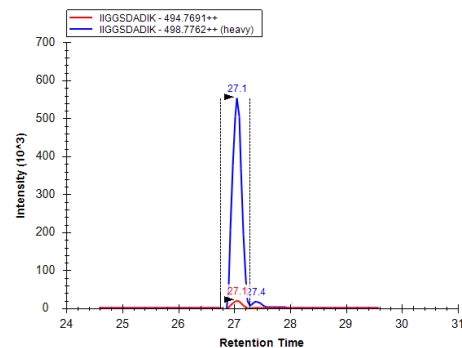
C1QC, L/H = 0.132



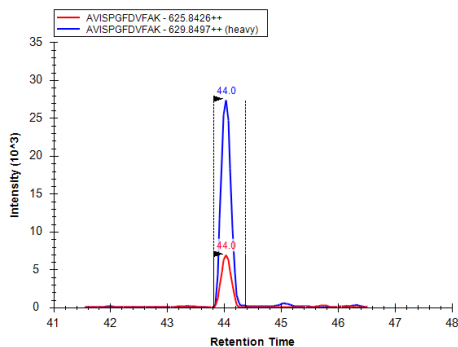
C1R, L/H = 7.496



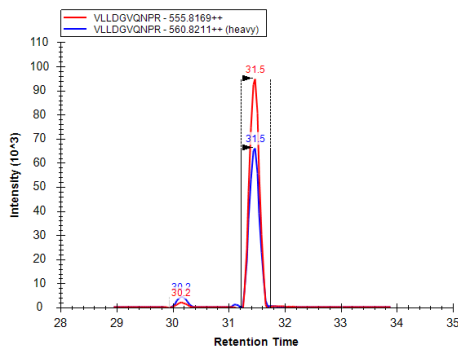
C1S, L/H = 0.037



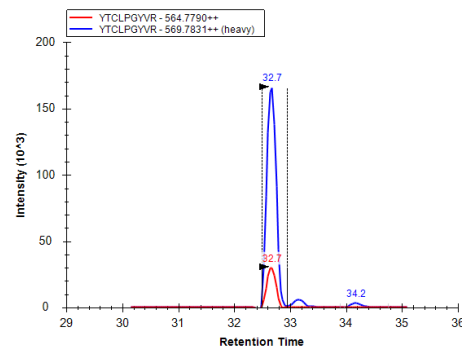
C2, L/H = 0.251



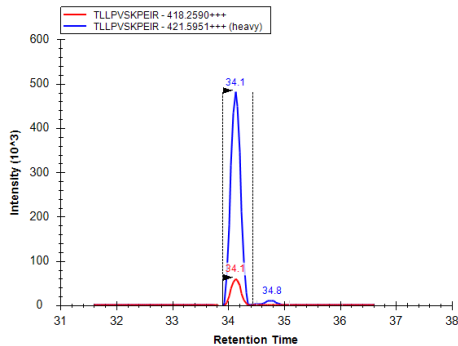
C3, L/H = 1.421



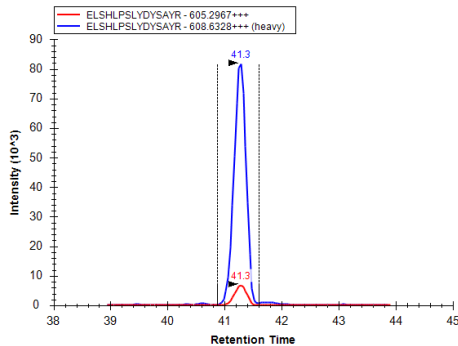
C4BPA, L/H = 0.174



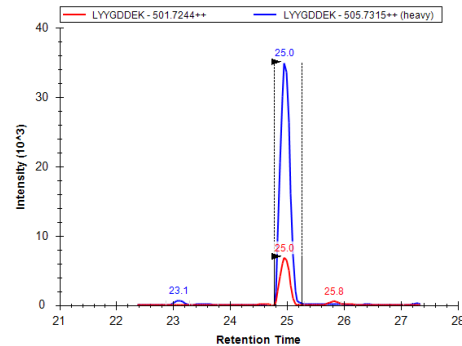
C5, L/H = 0.124



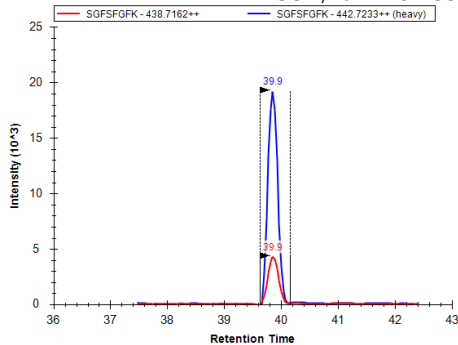
C7, L/H = 0.083



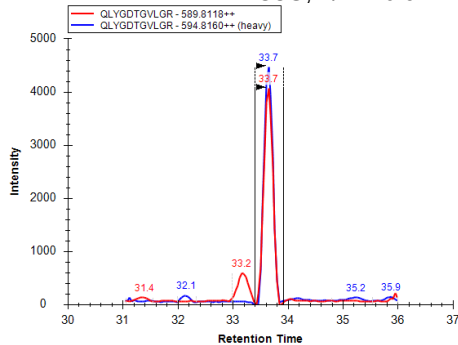
C8A, L/H = 0.187



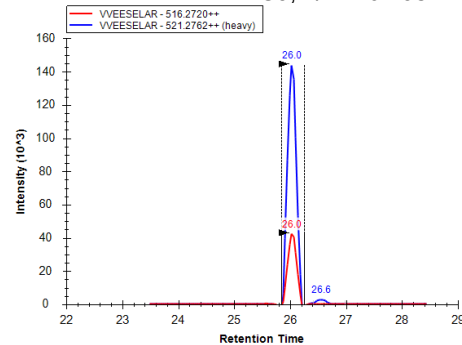
C8B, L/H = 0.233



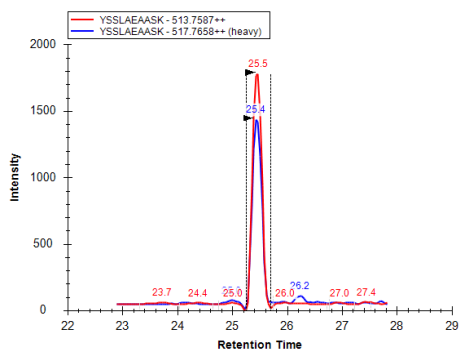
C8G, L/H = 0.921



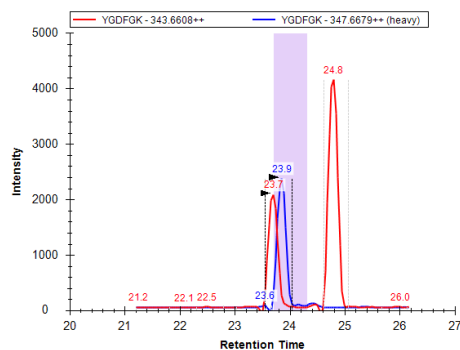
C9, L/H = 0.295



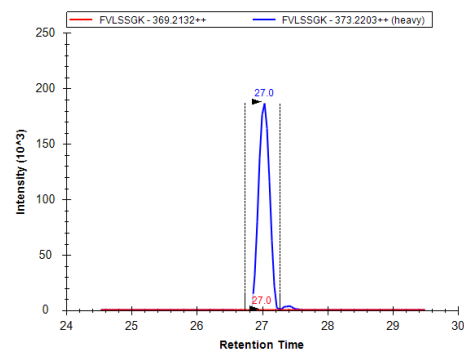
CA1, L/H = 1.224



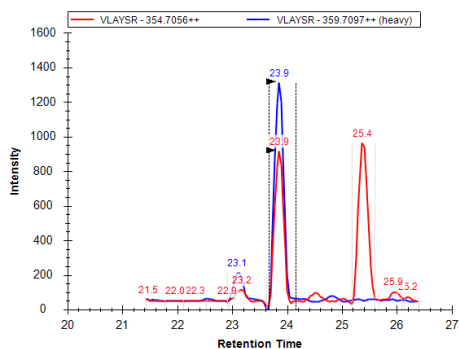
CA2, L/H = 0.943



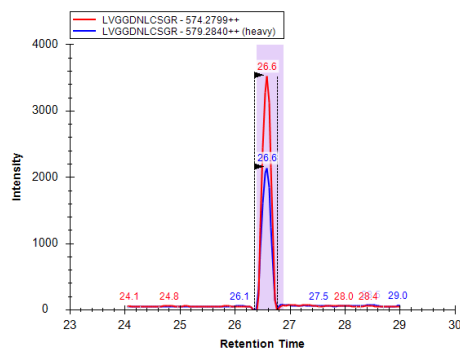
CALR, L/H = 0.002



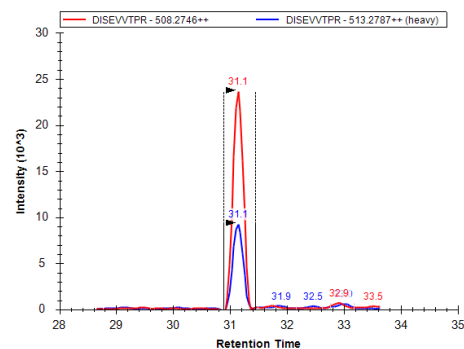
CD14, L/H = 0.66



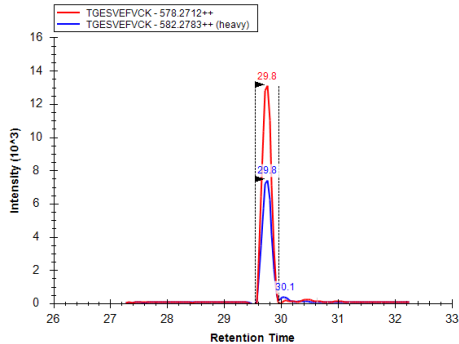
CD5L, L/H = 1.661



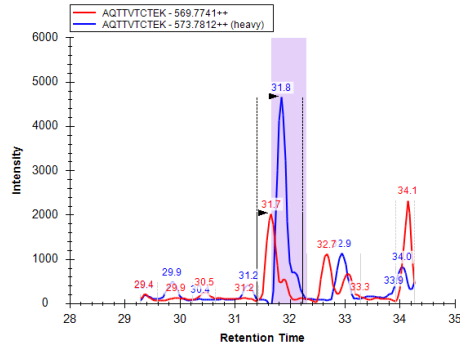
CFB, L/H = 2.583



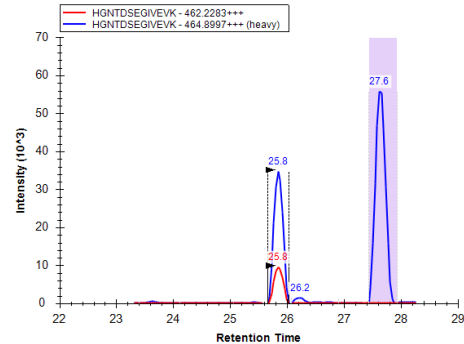
CFH, L/H = 1.777



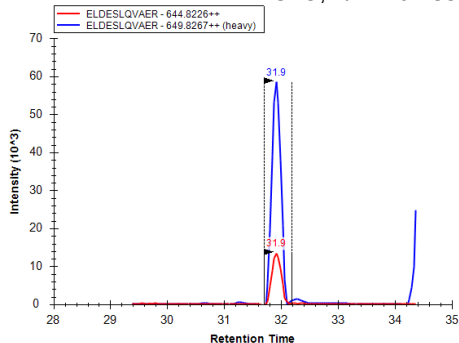
CFHR3, L/H = 0.298



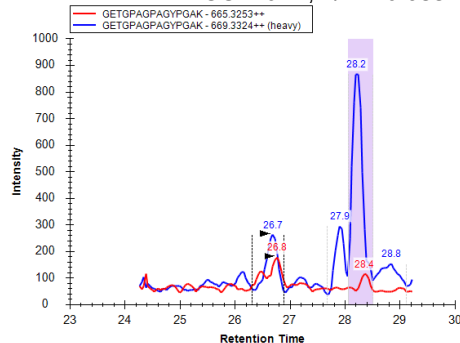
CFI, L/H = 0.275



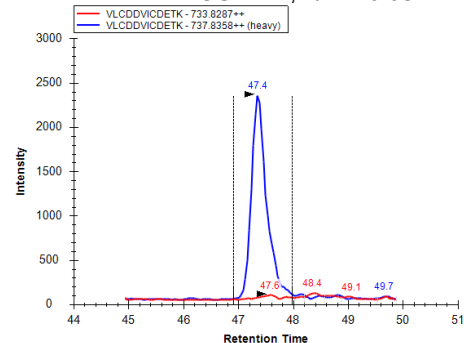
CLU, L/H = 0.235



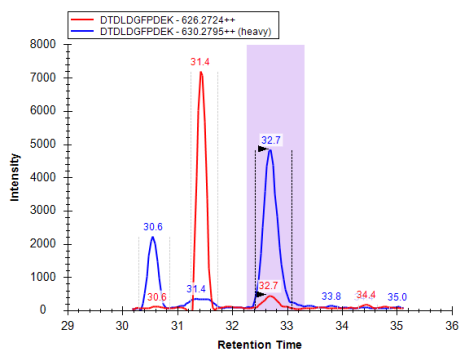
COL10A1, L/H = 0.683



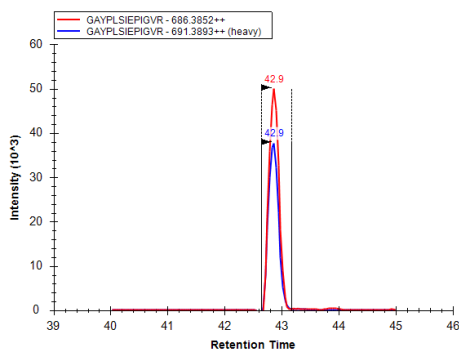
COL1A1, L/H = 0.037



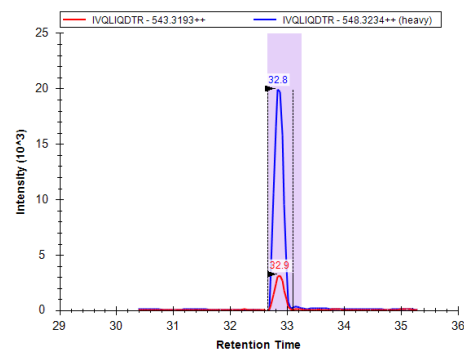
COMP, L/H = 0.092



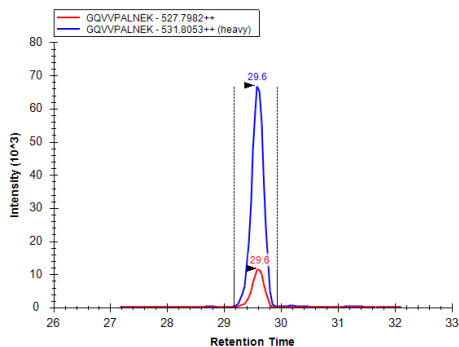
CP, L/H = 1.302



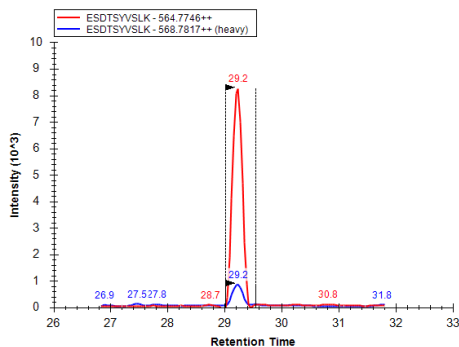
CPN1, L/H = 0.159



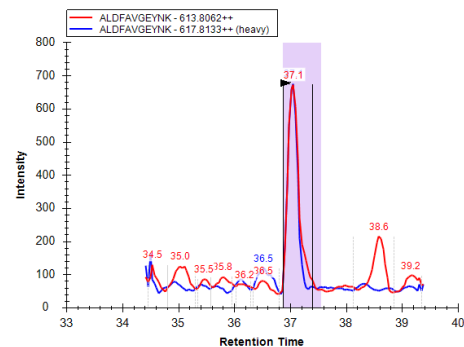
CPN2, L/H = 0.167



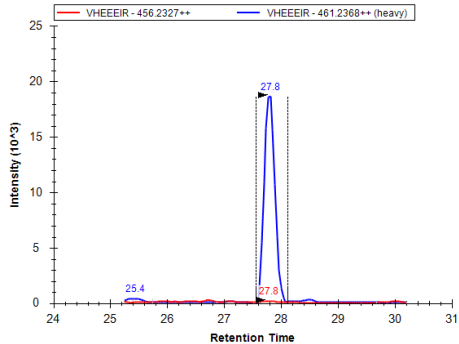
CRP, L/H = 10.399



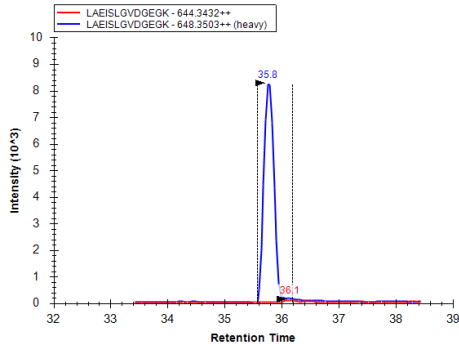
CST3, L/H = 1.141



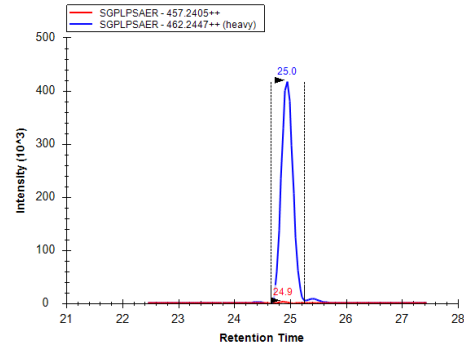
DES, L/H = 0.014



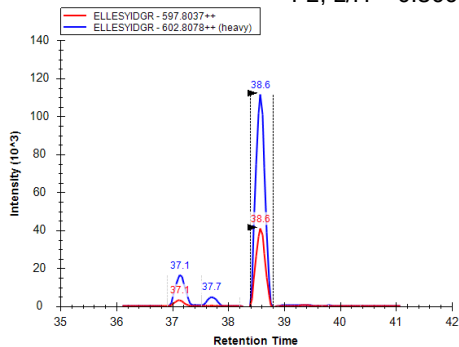
DSG3, L/H = 0.007



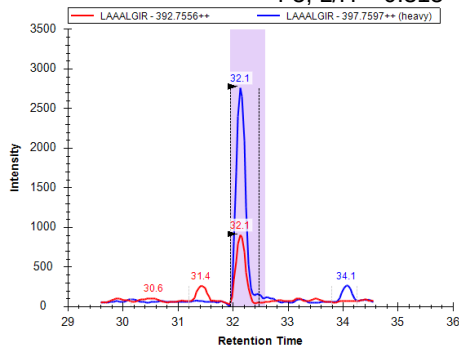
EXOSC10, L/H = 0.006



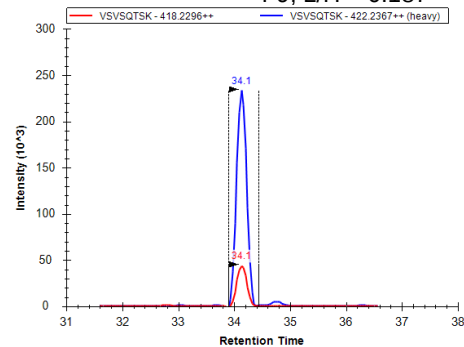
F2, L/H = 0.366



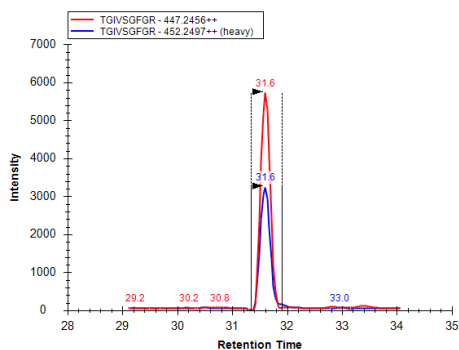
F5, L/H = 0.315



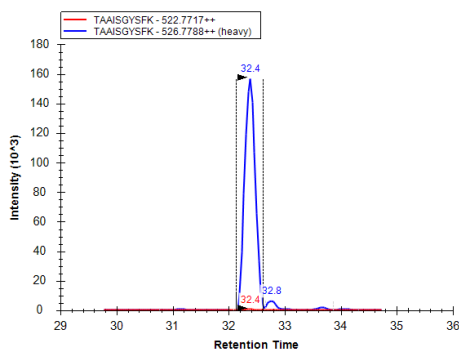
F9, L/H = 0.187



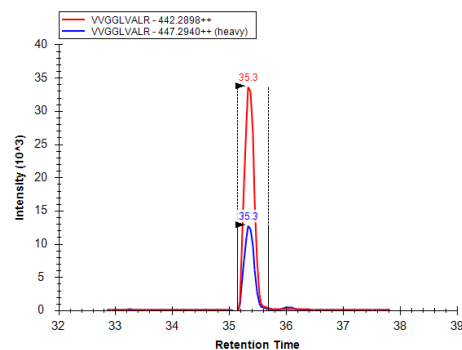
F10, L/H = 1.713



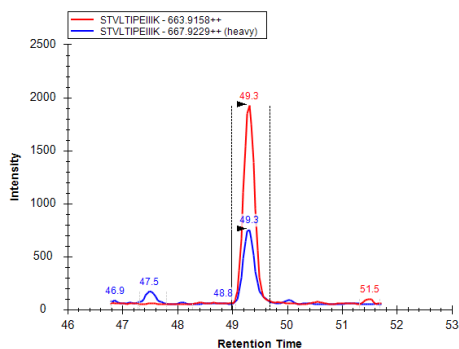
F11, L/H = 0.004



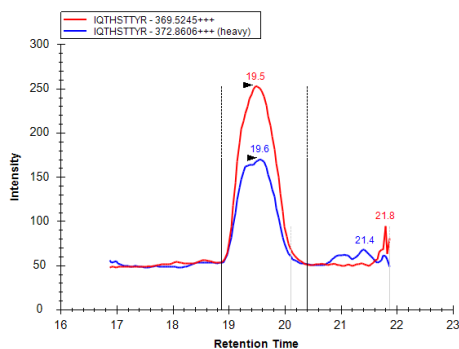
F12, L/H = 2.628



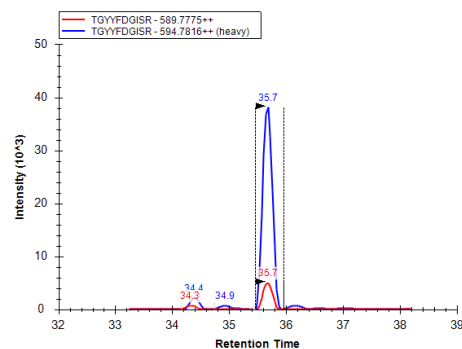
F13A1, L/H = 2.555



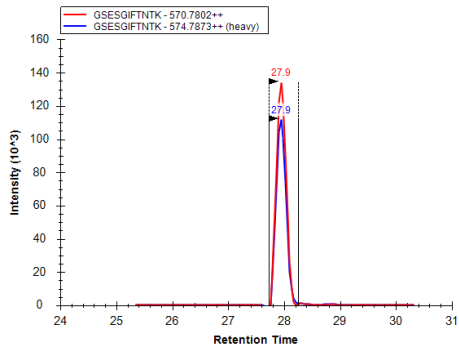
F13B, L/H = 1.732



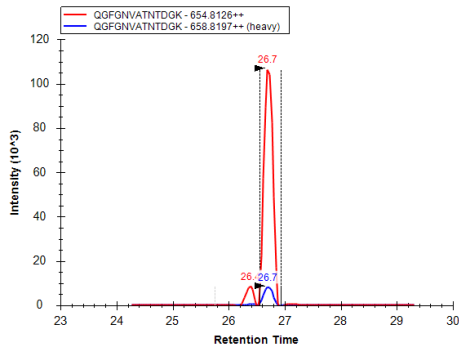
FBLN1, L/H = 0.125



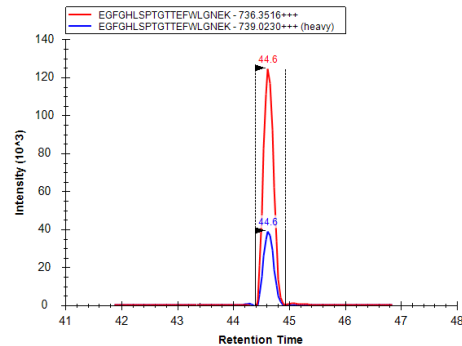
FGA, L/H = 1.191



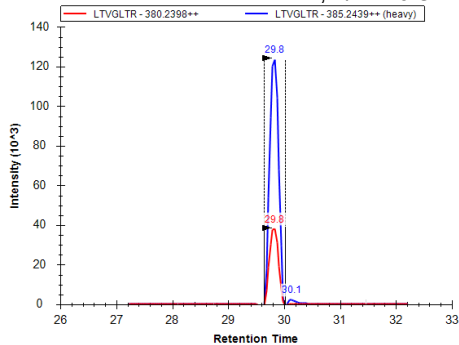
FGB, L/H = 12.945



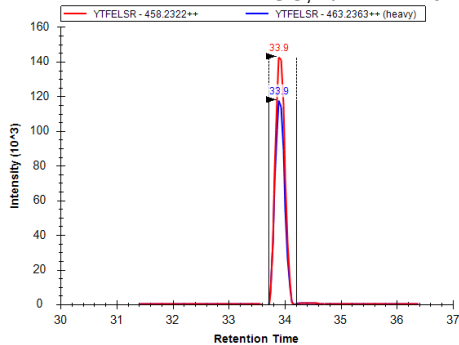
FGG, L/H = 3.288



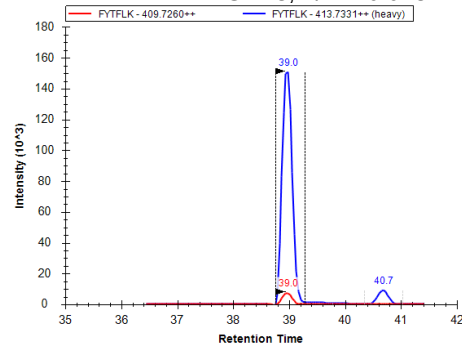
FN1, L/H = 0.311



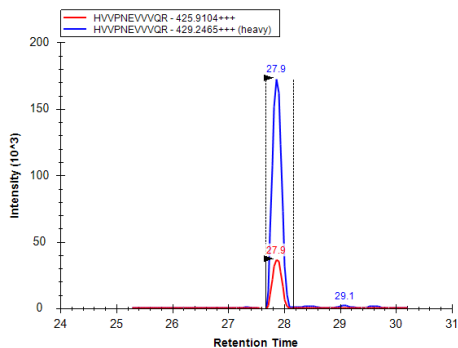
GC, L/H = 1.220



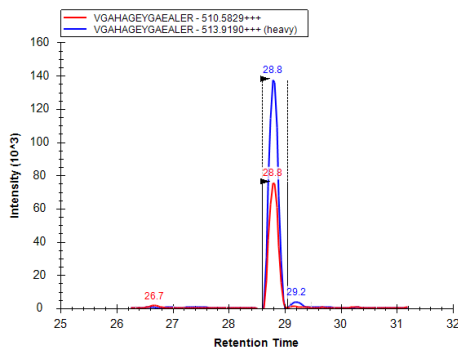
GPX3, L/H = 0.048



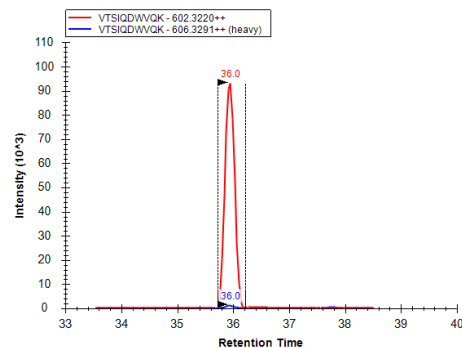
GSN, L/H = 0.205



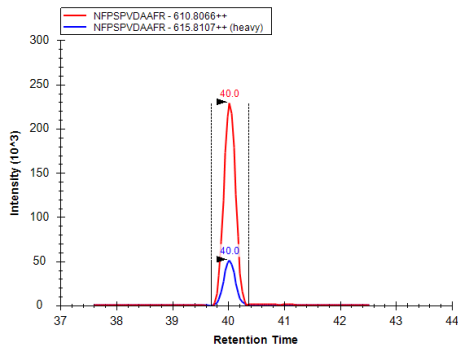
HBA1, L/H = 0.553



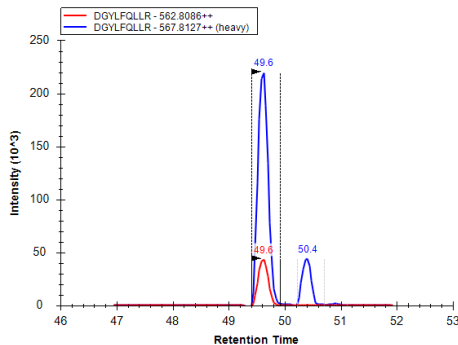
HP, L/H = 81.885



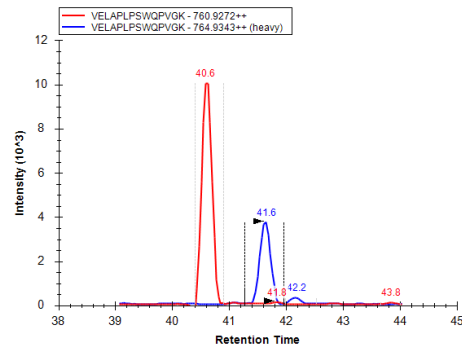
HPX, L/H = 4.597



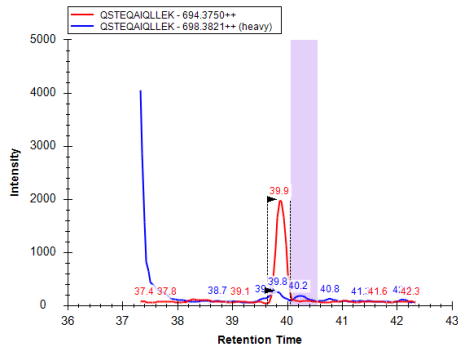
HRG, L/H = 0.193



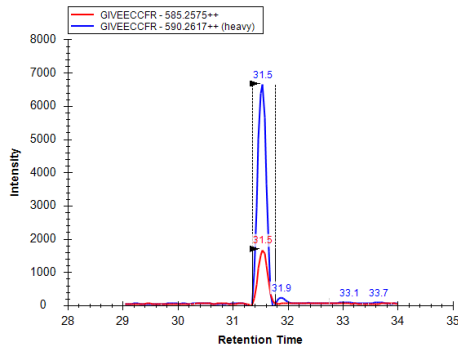
ICAM1, L/H = 0.045



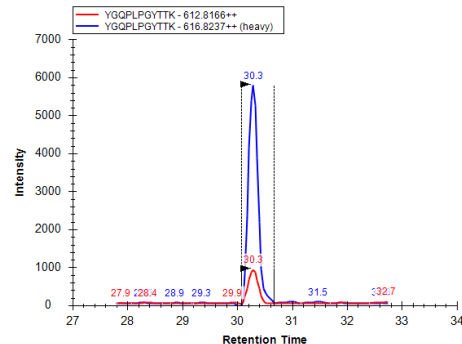
IDS, L/H = 7.768



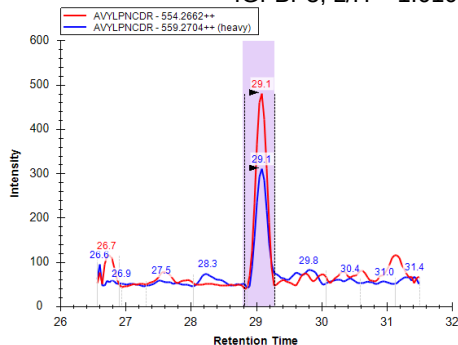
IGF2, L/H = 0.258



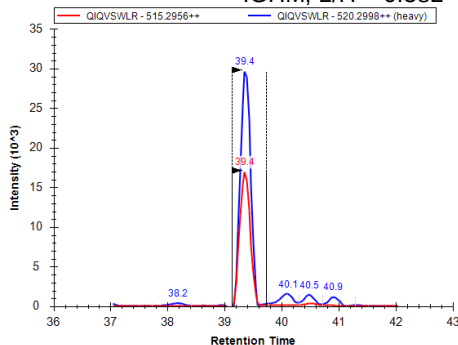
IGFBP3, L/H = 0.162



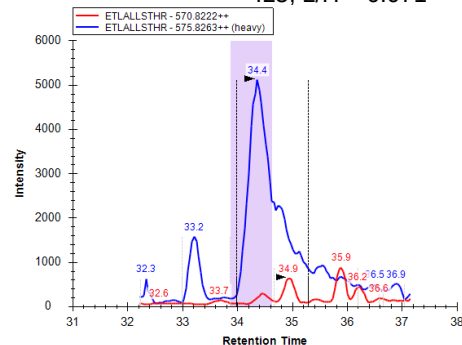
IGFBP5, L/H = 1.610



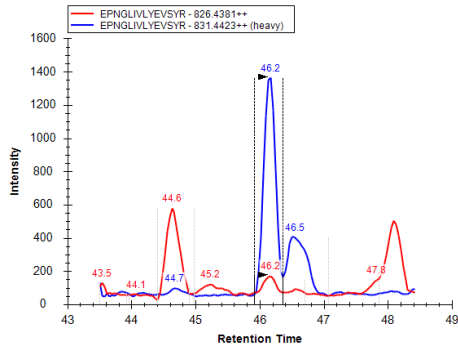
IGHM, L/H = 0.582



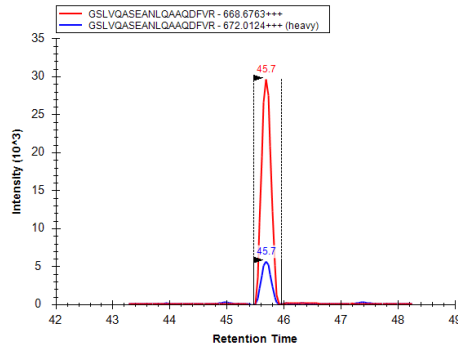
IL5, L/H = 0.071



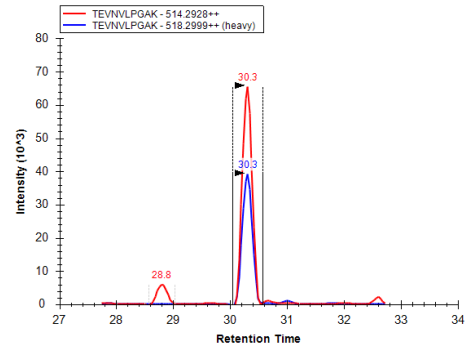
INSR, L/H = 0.104



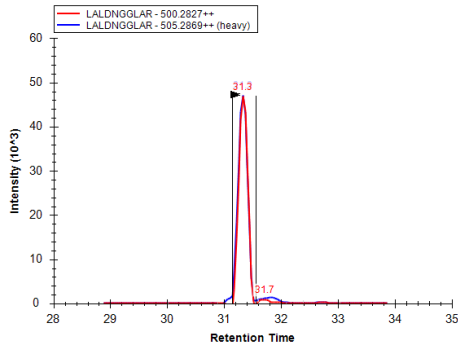
ITIH1, L/H = 5.249



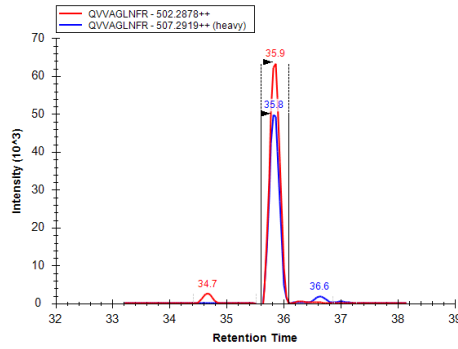
ITIH2, L/H = 1.647



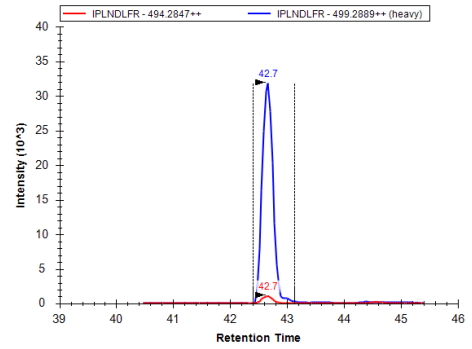
ITIH4, L/H = 0.994



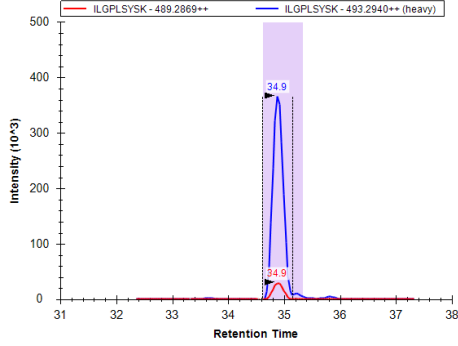
KNG1, L/H = 1.287



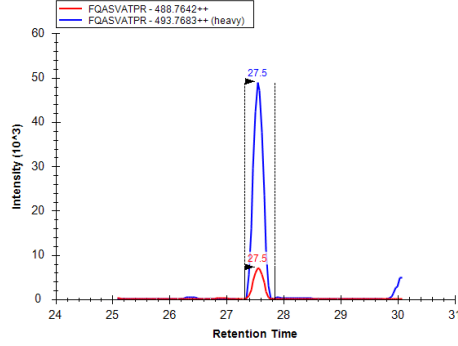
LAMP2, L/H = 0.030



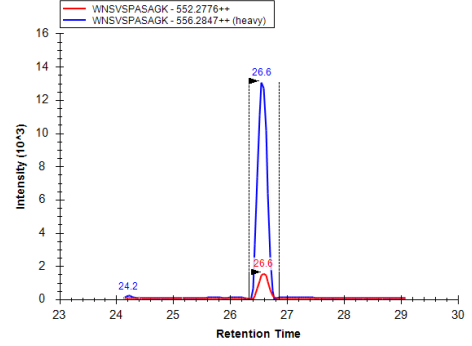
LUM, L/H = 0.081



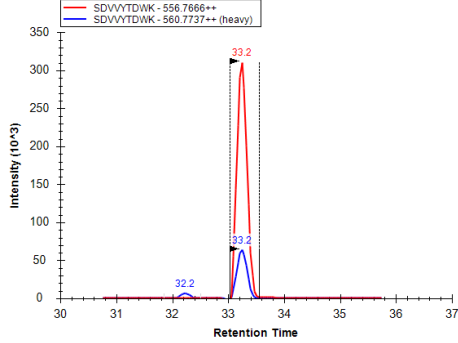
MBL2, L/H = 0.144



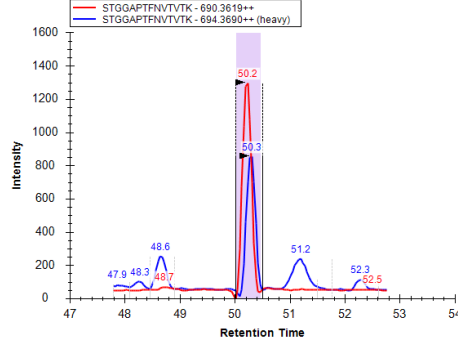
MTDH, L/H = 0.117



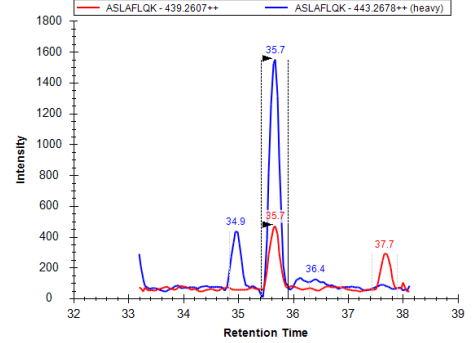
ORM1, L/H = 4.846



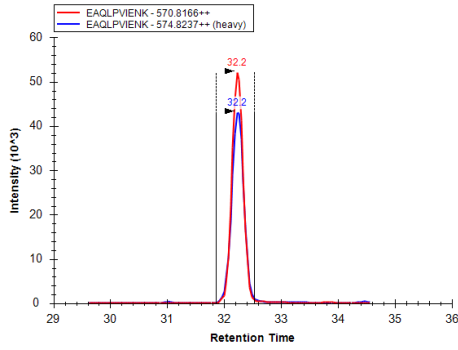
PFN1, L/H = 1.560



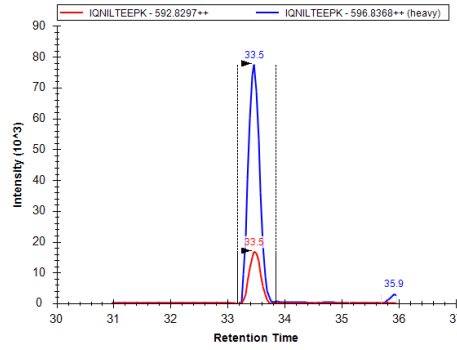
PLA2G7, L/H = 0.300



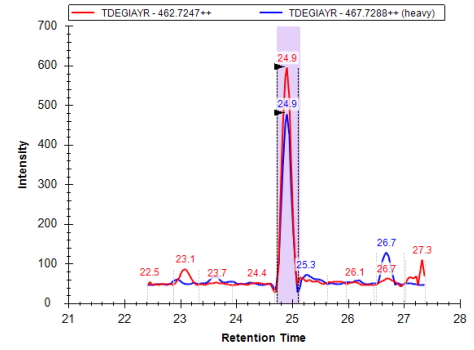
PLG, L/H = 1.125



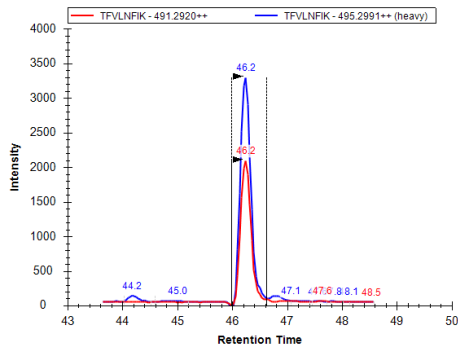
PON1, L/H = 0.217



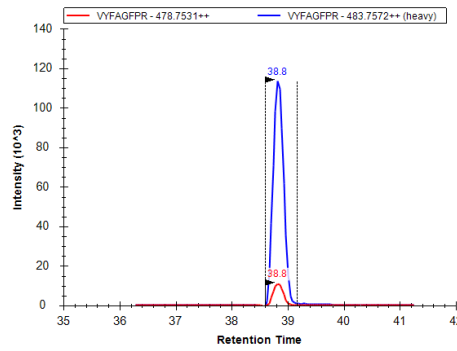
PRDX2, L/H = 1.274



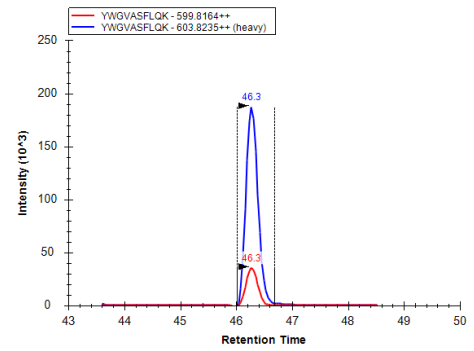
PROC, L/H = 0.625



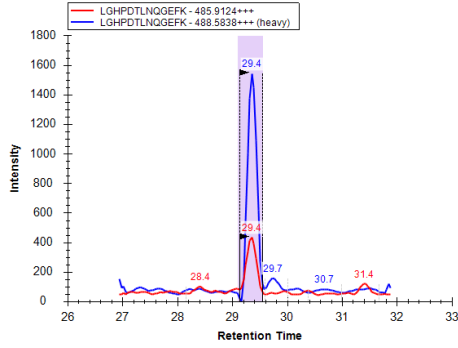
PROS1, L/H = 0.092



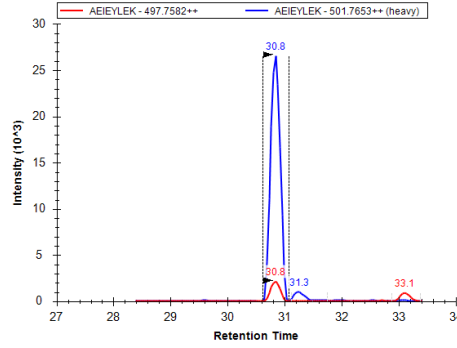
RBP4, L/H = 0.184



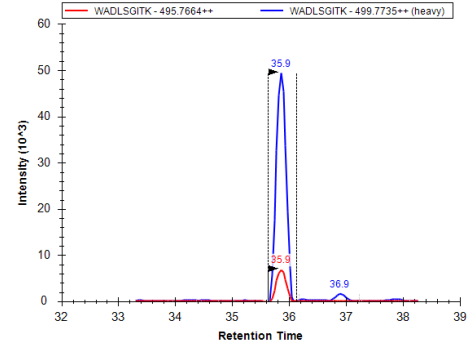
S100A9, L/H = 0.282



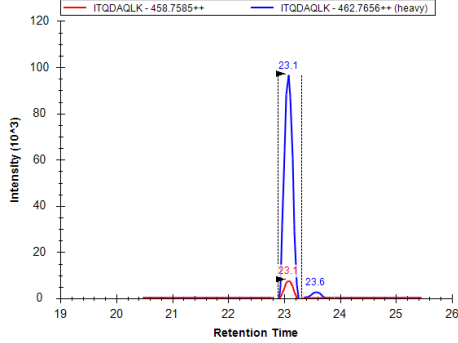
SELL, L/H = 0.076



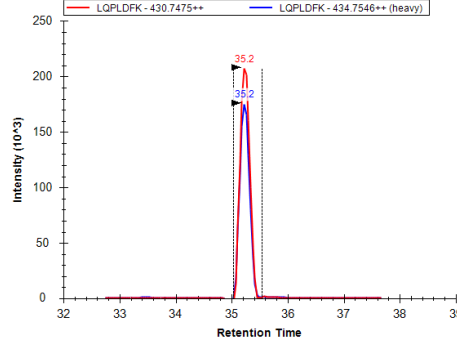
SERPINA4, L/H = 0.135



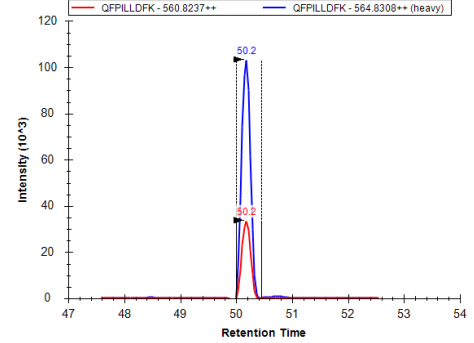
SERPINA6, L/H = 0.080



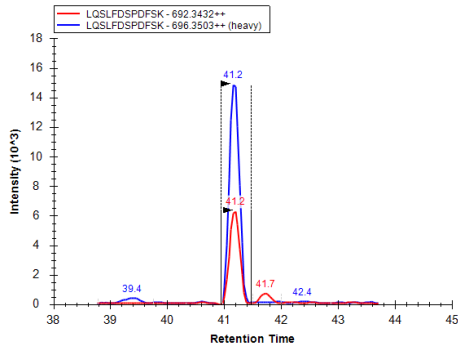
SERPINC1, L/H = 1.176



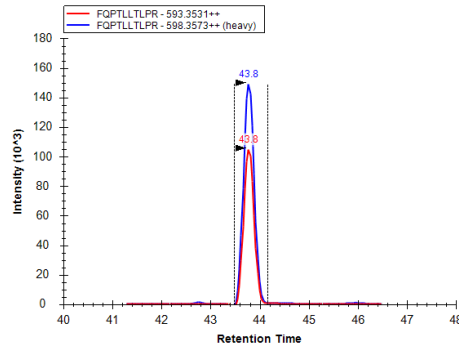
SERPIND1, L/H = 0.322



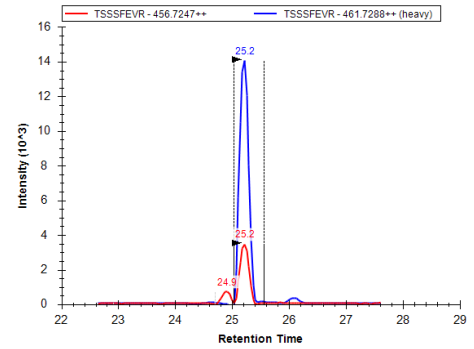
SERPINF1, L/H = 0.415



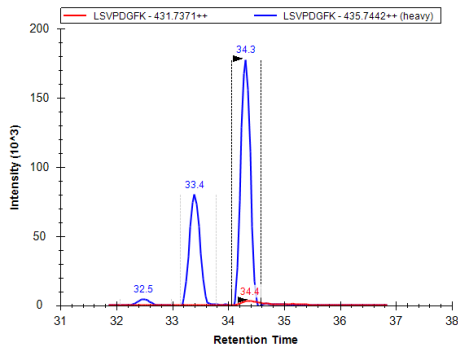
SERPING1, L/H = 0.685



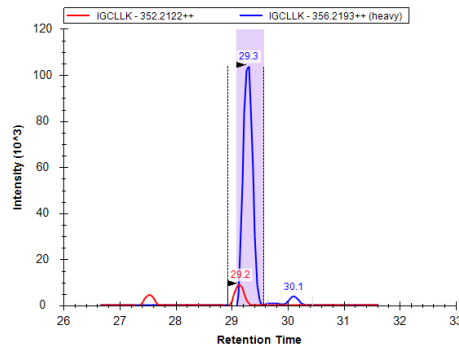
SHBG, L/H = 0.239



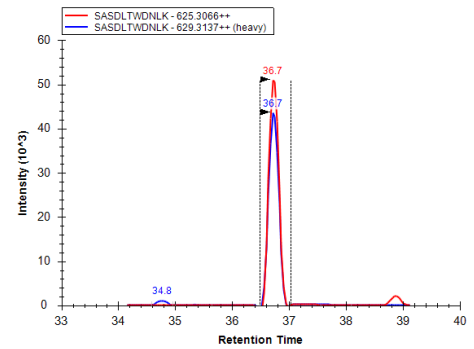
SLC4A1, L/H = 0.031



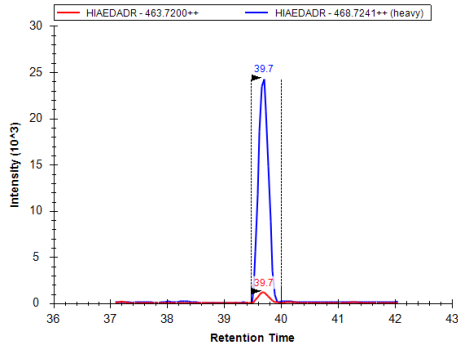
SSB, L/H = 0.072



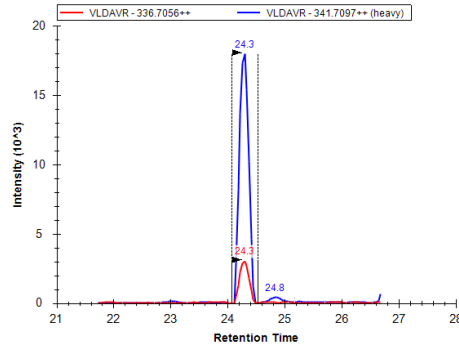
TF, L/H = 1.160



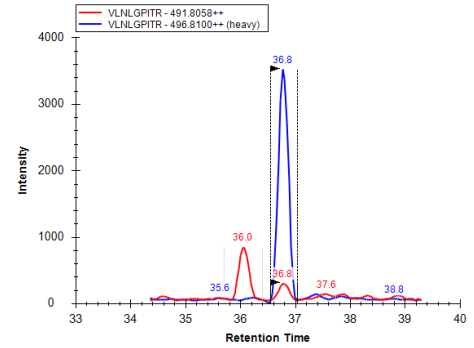
TPM1, L/H = 0.048



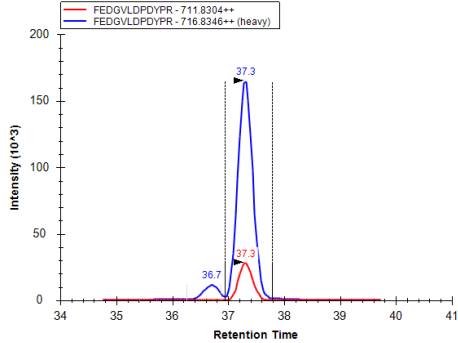
TTR, L/H = 0.169



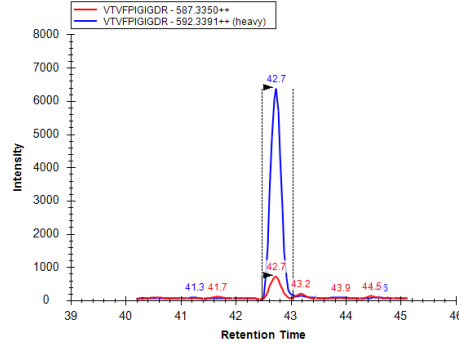
UMOD, L/H = 0.077

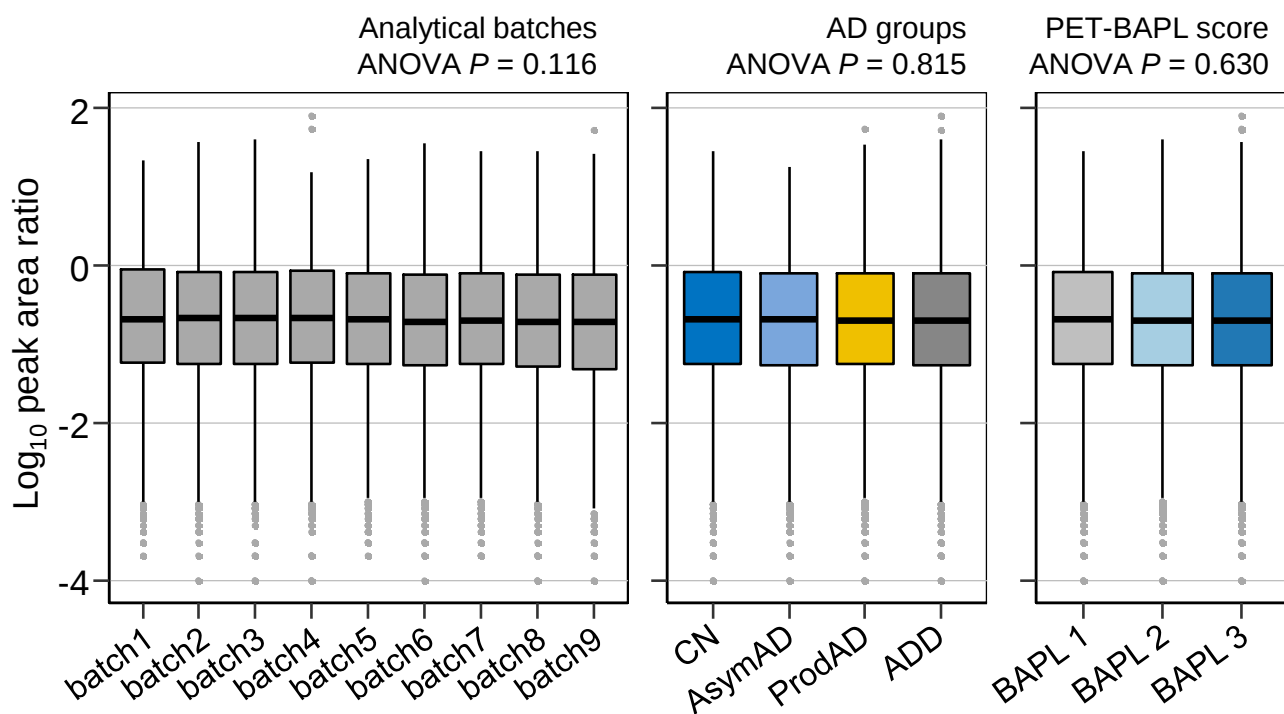


VTN, L/H = 0.161

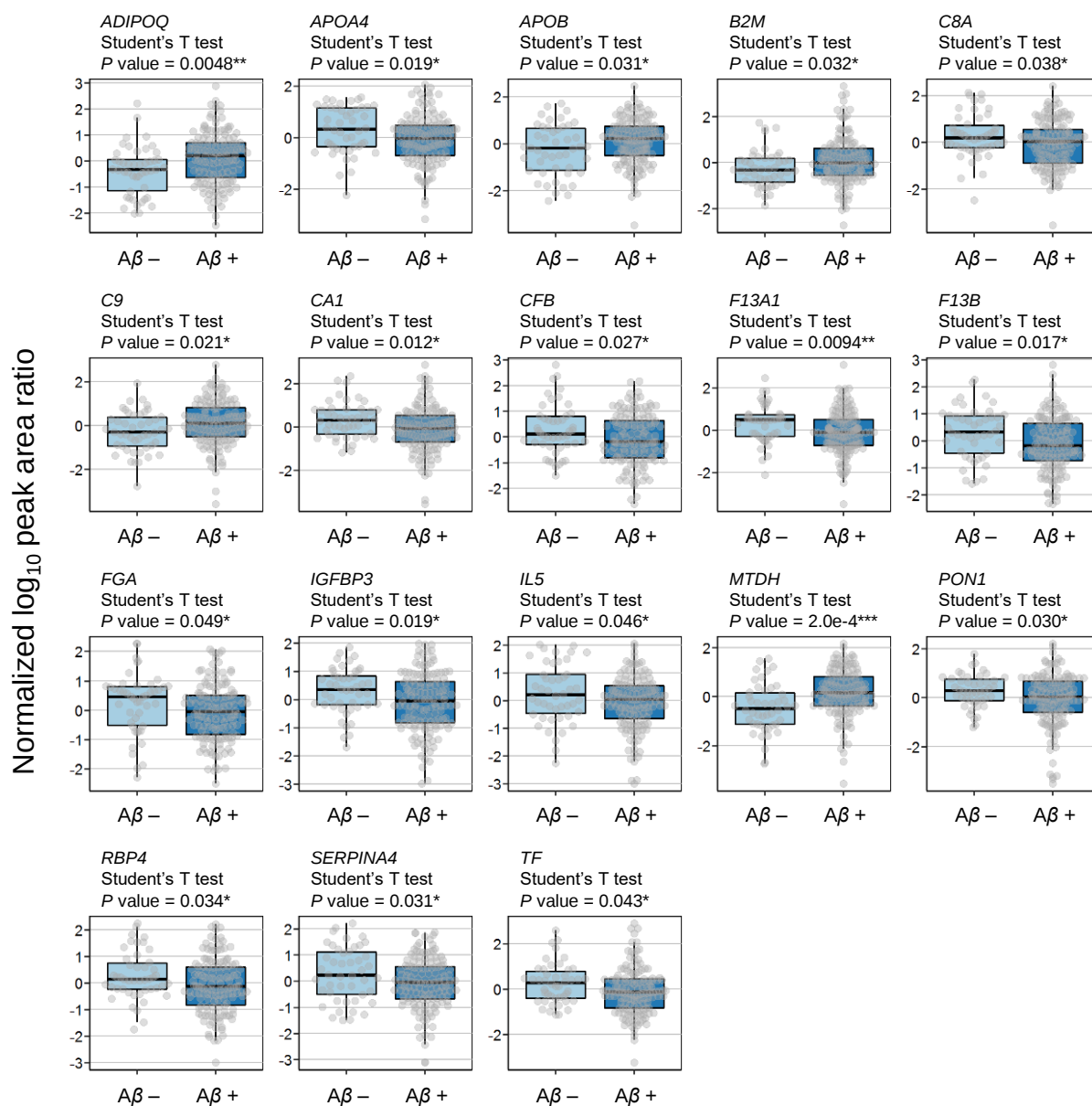


VWF, L/H = 0.107





Supplementary Figure S2. Variation of overall 119 proteins levels in analytical batches, AD groups, and PET-BAPL score groups. Peak area ratios of 119 proteins from 185 subjects were measured by MRM-MS; their distribution between batches, cognitive control and AD patient groups, and BAPL scores are shown in box plots. Significance of differences in protein peak area ratios between groups was measured by one-way ANOVA.



Supplementary Figure S3. The 18 differentially expressed proteins in PET-BAPL score groups. Box plots of 18 DEPs in the PET-BAPL groups: Amyloid- β -negative (PET-BAPL 1) and Amyloid- β -positive (PET-BAPL 2-3). Significant differences in protein expression of BAPL groups were measured by student's t-test, and significance levels are represented as “*” for $P < 0.05$; “**” for $P < 0.01$; and “***” for $P < 0.001$.

Prediction (APOE ε4)					
		AsymAD	ProdAD	ADD	TPR
References	AsymAD	0.0% (±0.0%)	17.2% (±3.0%)	10.8% (±3.0%)	0.0% (±0.0%)
	ProdAD	0.0% (±0.0%)	18.0% (±3.4%)	18.0% (±3.4%)	50.0% (±9.5%)
	ADD	0.0% (±0.0%)	22.3% (±0.9%)	13.7% (±0.6%)	38.0% (±2.0%)
	FPR	NA	70.0% (±3.0%)	65.0% (±5.4%)	

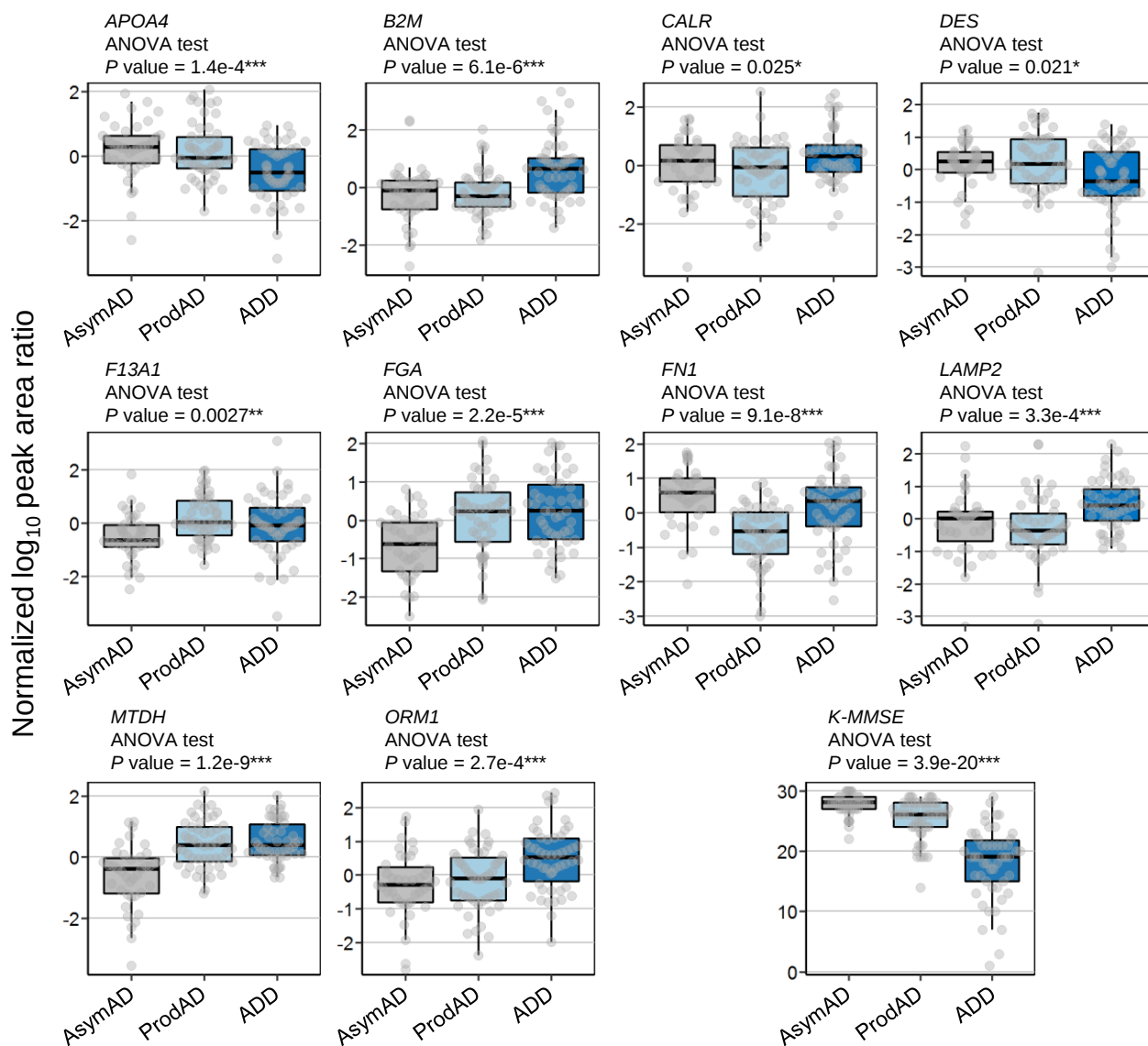
Prediction (K-MMSE)					
		AsymAD	ProdAD	ADD	TPR
References	AsymAD	5.8% (±1.8%)	21.5% (±2.5%)	0.7% (±0.7%)	20.7% (±6.6%)
	ProdAD	2.9% (±1.8%)	26.6% (±1.3%)	6.5% (±0.7%)	74.0% (±4.0%)
	ADD	0.0% (±0.0%)	7.9% (±1.7%)	28.1% (±1.8%)	78.0% (±4.9%)
	FPR	22.5% (±11.8%)	52.3% (±1.0%)	20.3% (±2.8%)	

Prediction (10 proteins, CV)					
		AsymAD	ProdAD	ADD	TPR
References	AsymAD	18.7% (±1.3%)	5.1% (±0.9%)	4.3% (±1.3%)	66.8% (±4.8%)
	ProdAD	4.3% (±1.8%)	28.8% (±1.9%)	2.9% (±1.3%)	80.0% (±5.5%)
	ADD	3.6% (±1.1%)	5.0% (±1.4%)	27.4% (±2.0%)	76.0% (±5.1%)
	FPR	27.0% (±7.6%)	25.6% (±1.9%)	20.9% (±3.0%)	

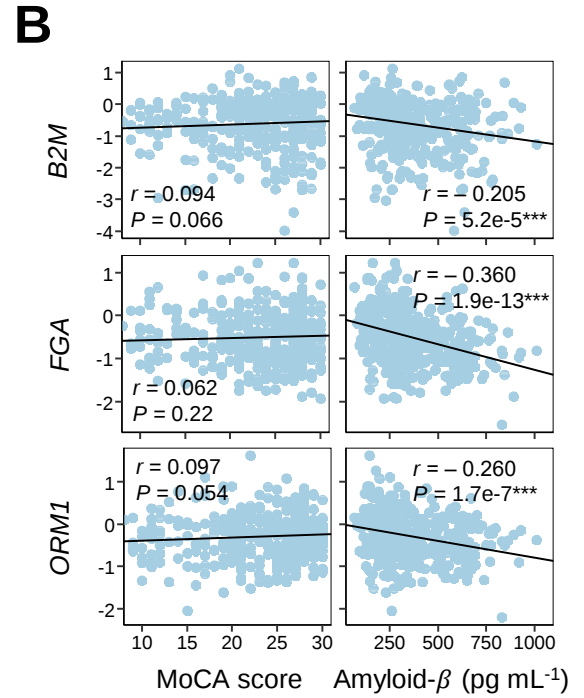
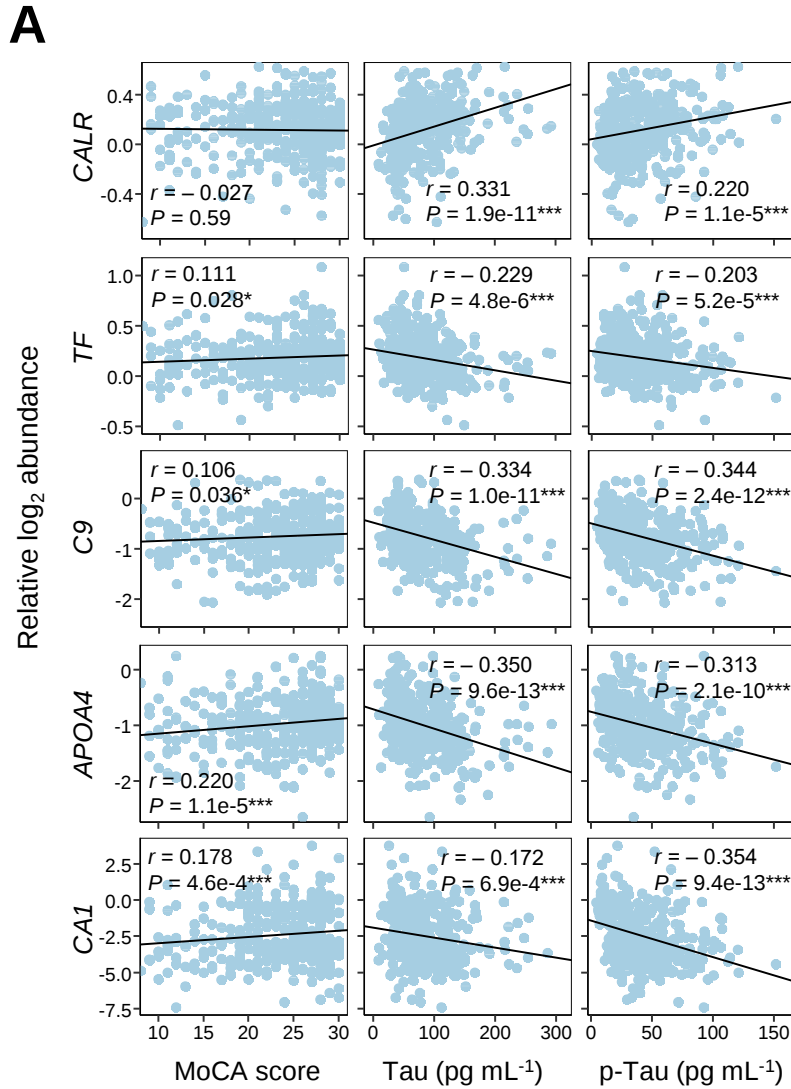
Prediction (10 proteins with K-MMSE)					
		AsymAD	ProdAD	ADD	TPR
References	AsymAD	20.2% (±2.3%)	4.3% (±1.3%)	3.6% (±1.6%)	72.5% (±9.2%)
	ProdAD	5.8% (±2.2%)	28.0% (±2.0%)	2.1% (±1.4%)	78.0% (±5.8%)
	ADD	2.2% (±0.9%)	2.9% (±1.4%)	30.9% (±1.7%)	86.0% (±5.1%)
	FPR	26.6% (±4.3%)	19.8% (±3.5%)	14.3% (±4.2%)	

Prediction (10 proteins, nCV)					
		AsymAD	ProdAD	ADD	TPR
References	AsymAD	19.4% (±0.8%)	6.5% (±1.8%)	2.1% (±1.4%)	69.3% (±2.8%)
	ProdAD	3.6% (±2.0%)	26.7% (±3.3%)	5.7% (±1.8%)	74.0% (±8.7%)
	ADD	4.3% (±1.4%)	5.1% (±1.8%)	26.6% (±2.1%)	74.0% (±6.0%)
	FPR	28.5% (±3.9%)	29.0% (±5.5%)	19.8% (±6.3%)	

Supplementary Figure S4. Confusion matrix of prediction results of APOE genotyping, K-MMSE, the 10-protein models by CV and nested CV, and the model with 10 proteins and K-MMSE score. Prediction results of the 5 models for assessing neurocognitive impairments using data from the analysis of the 139 individual samples. Gray squares contain correct prediction results, and the proportion of classifications with 95% confidence intervals is shown. True positive rates (TPRs) and false positive rates (FPRs) for each group are presented in the matrices to show the diagnostic performance of the 5 models.



Supplementary Figure S5. Box plots of the 11 features in the final APM model. Relative plasma protein levels of the 10 proteins from asymptomatic AD (AsymAD) group, prodromal AD (ProdAD) group, and ADD group were measured by MRM-MS. K-MMSE scores of the subjects were measured and included in the final model. P -values for the comparison of protein levels and K-MMSE scores from the 3 groups were calculated by ANOVA. Significance levels are represented as “#” for $P < 0.1$; “**” for $P < 0.01$; and “***” for $P < 0.001$. Box plots represent the first, second, and third quartiles, and whiskers represent the 1.5 x interquartile range (IQR).



Supplementary Figure S6. CSF levels of proteins in the external CSF cohorts. Relative CSF levels of the proteins and their correlation with the original tests, such as cognitive score (MoCA), amyloid- β level, total tau level, and phospho-tau level in the CSF cohort [Cohort 1 (N = 297) and Cohort2 (N = 96) from Johnson et al.]. Pearson's correlation was used to measure the correlation between protein levels and original tests. Significance levels are indicated as “*” for $P < 0.05$; “**” for $P < 0.01$; and “***” for $P < 0.001$.