

### Supporting Information

#### **A two-trick pony: lysosomal protease cathepsin B possesses surprising ligase activity**

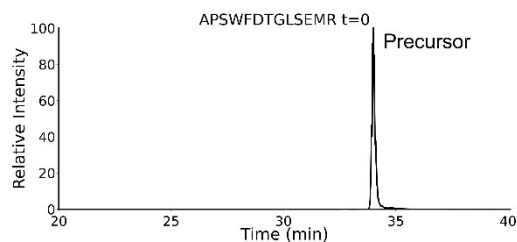
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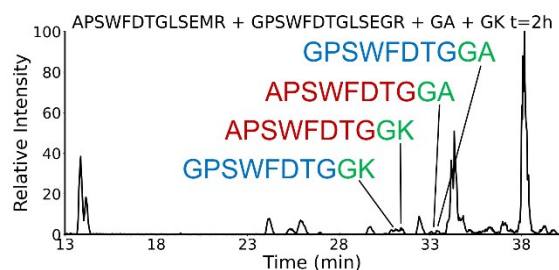
<sup>‡</sup>Department of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, Department of Chemistry, Dornsife College of Letters, Arts and Sciences, Norris Comprehensive Cancer Center, and Research Center for Liver Diseases, University of Southern California, Los Angeles, California 90089, United States

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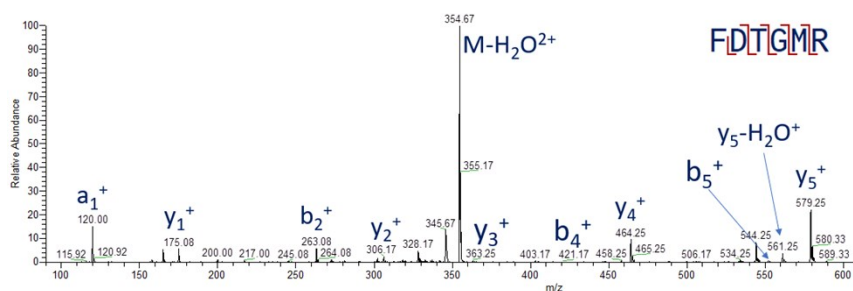
E-mail: [ryan.julian@ucr.edu](mailto:ryan.julian@ucr.edu)



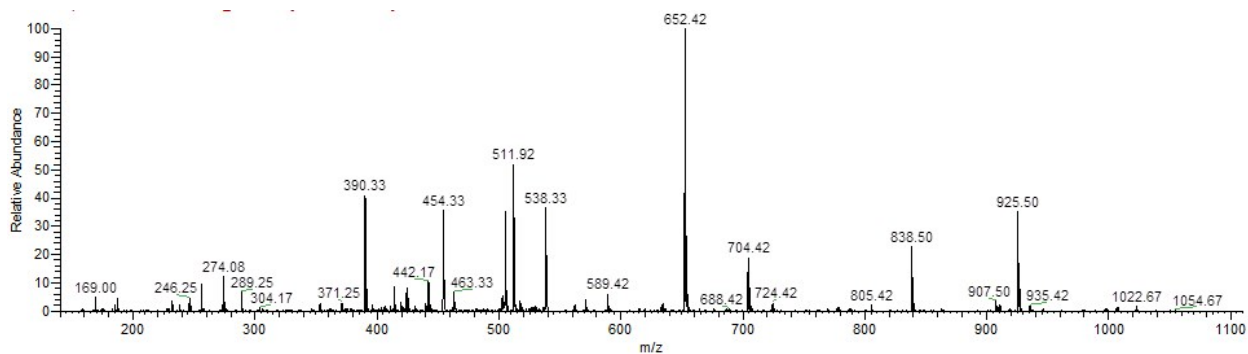
**Figure S1.** LC chromatogram for the initial timepoint of APSWFD TGLSEMR + CatB. No peaks were present except for the precursor peptide.



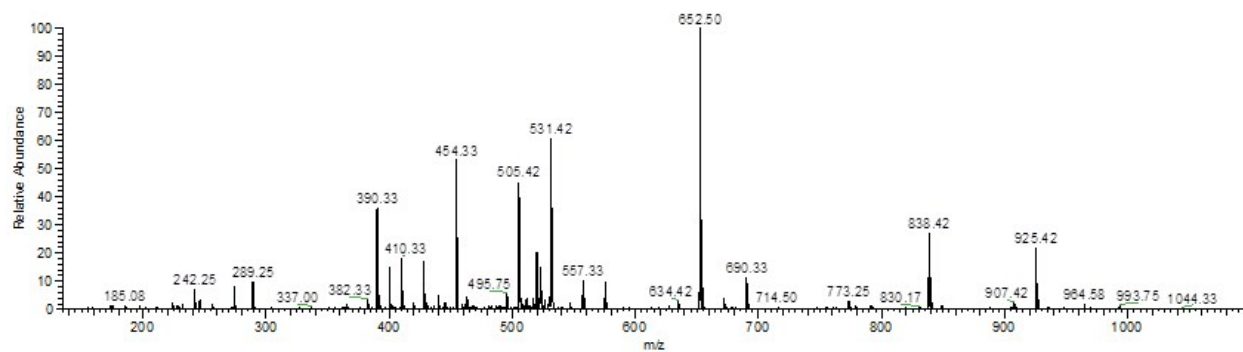
**Figure S2.** LC chromatogram for the incubation of APSWFD TGLSEMR and GPSWFD TGLSEGR with dipeptides GA and GK with CatB. Raw data for the results shown in Figure 4.



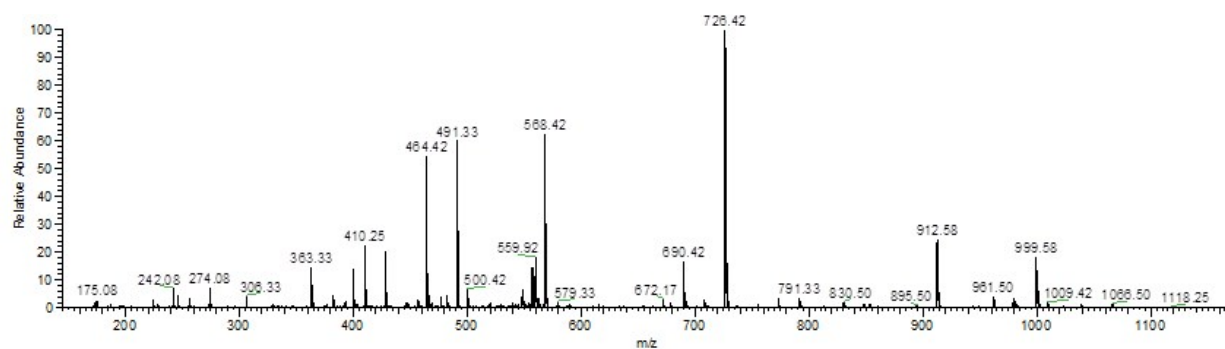
**Figure S3.** CID fragmentation spectrum for the ligation product FDTGMR.



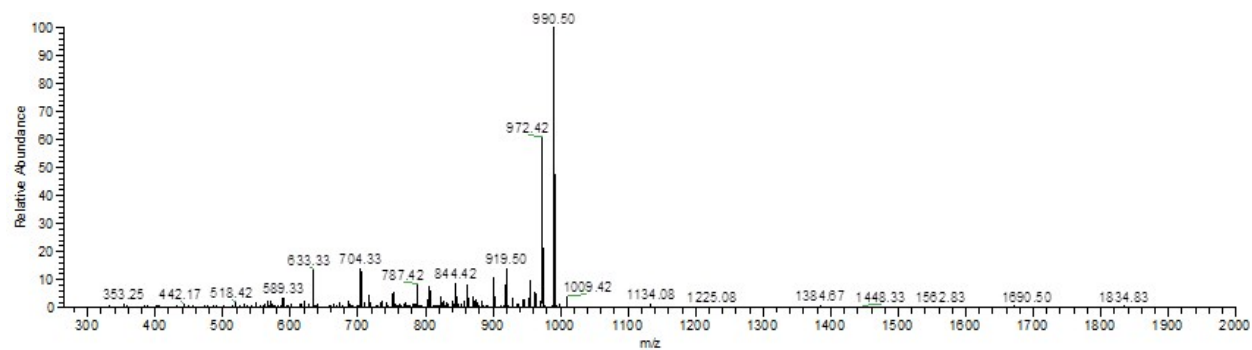
**Figure S4.** CID fragmentation spectrum for the ligation product APSWFD TGGR shown in Figure 3.



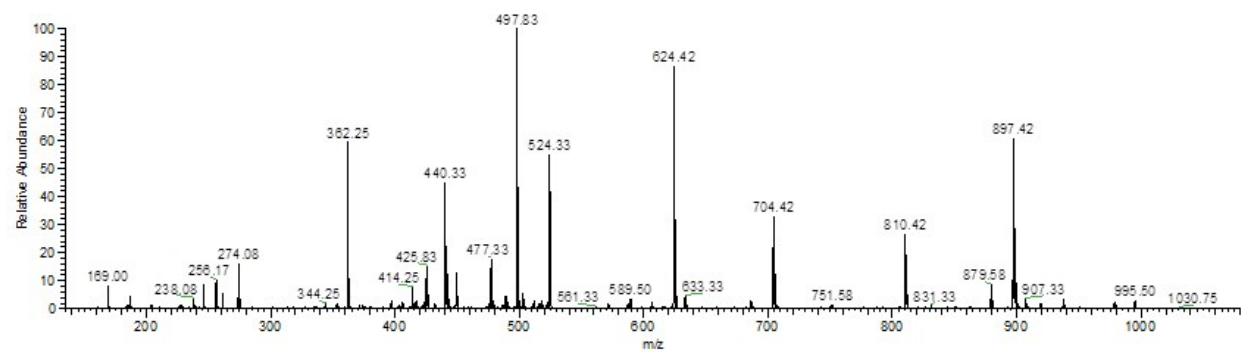
**Figure S5.** CID fragmentation spectrum for the ligation product GPSWFDTGGR shown in Figure 3.



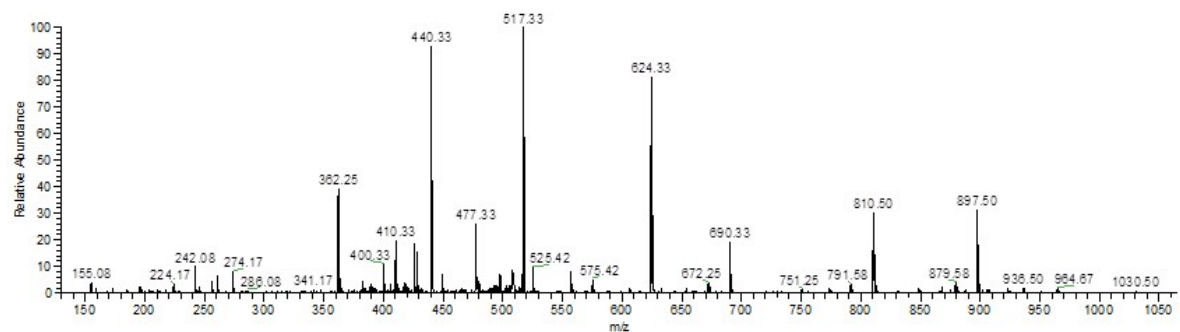
**Figure S6.** CID fragmentation spectrum for the ligation product GPSWFDTGMR shown in Figure 3.



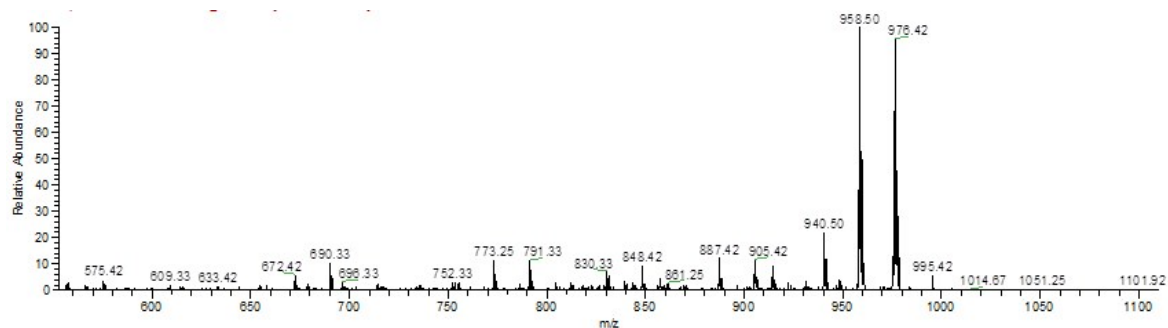
**Figure S7.** CID fragmentation spectrum for the ligation product APSWFDTGGA shown in Figure 4.



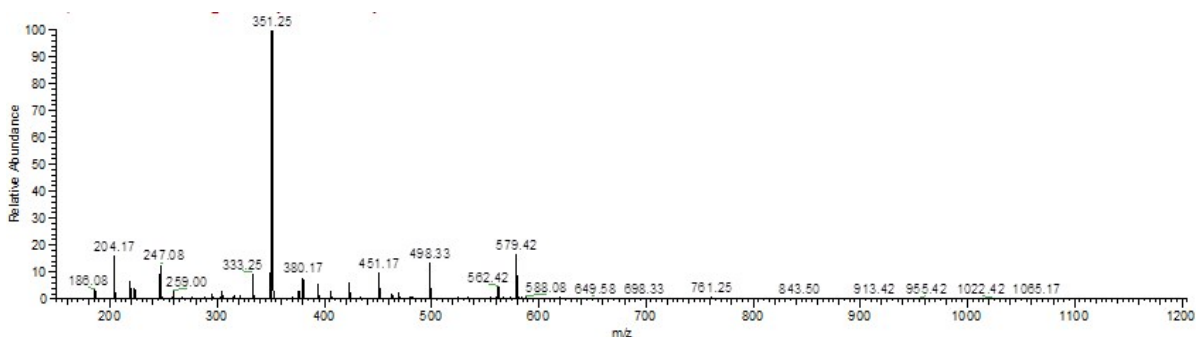
**Figure S8.** CID fragmentation spectrum for the ligation product APSWFDTGGK shown in Figure 4.



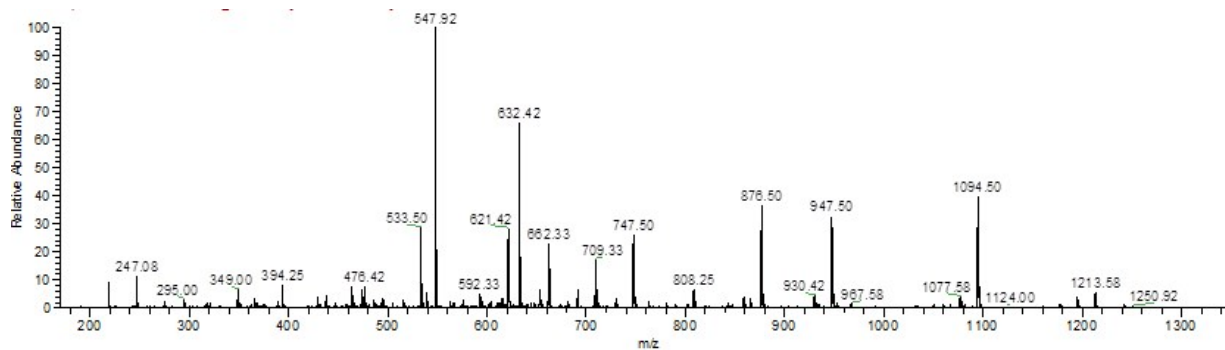
**Figure S9.** CID fragmentation spectrum for the ligation product GPSWFDTGGK shown in Figure 4.



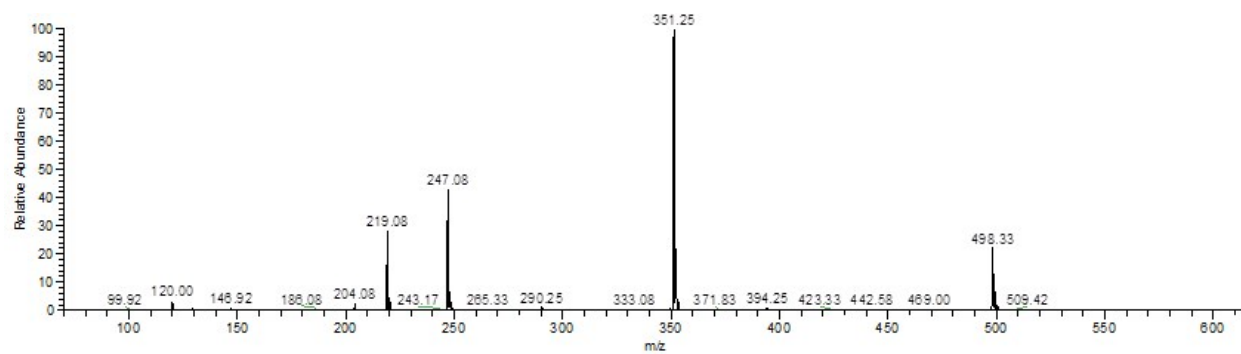
**Figure S10.** CID fragmentation spectrum for the ligation product GPSWFDTGGA shown in Figure 4.



**Figure S11.** CID fragmentation spectrum for the ligation product VFFGA shown in Figure 5.



**Figure S12.** CID fragmentation spectrum for the ligation product VFFAEDVGSNKGA shown in Figure 5.



**Figure S13.** CID fragmentation spectrum for the ligation product VFFGK shown in Figure 5.