Supplementary Tables

Table S1: Deuterium Incorporation for FXIII at One Minute

Residues	Theo. D_{max} [a]	Zymogen	$FXIIIa^{Ca}$	K9 DON $FXIIIa^{Ca}$	IAA $FXIIIa^{Ca}$	$FXIIIa^{IIa}$	K9 DON $FXIIIa^{IIa}$	IAA $FXIIIa^{IIa}$
98-104	6.5	4.4 ± 0.0	2.9 ± 0.1	3.4 ± 0.1	2.4 ± 0.1	n/a	n/a	n/a
220-230	10.8	2.4 ± 0.1	2.9 ± 0.1	3.1 ± 0.1	2.5 ± 0.1	2.8 ± 0.1	3.0 ± 0.0	3.1 ± 0.1
240-247	7.5	1.2 ± 0.0	1.7 ± 0.1	1.7 ± 0.0	1.7 ± 0.1	1.6 ± 0.0	1.7 ± 0.0	1.7 ± 0.1
248-264	15.9	2.9 ± 0.0	n/a	n/a	n/a	3.8 ± 0.0	3.8 ± 0.0	3.9 ± 0.1
513-522	9.7	3.8 ± 0.0	2.7 ± 0.0	2.9 ± 0.0	2.3 ± 0.1	3.3 ± 0.1	3.1 ± 0.0	3.1 ± 0.2
526-546	21.2	12.8 ± 0.1	7.7 ± 0.2	n/a	n/a	12.3 ± 0.1	10.7 ± 0.3	12.0 ± 0.5
535-541	6.5	0.6 ± 0.0	0.7 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.8 ± 0.1

FXIII, Factor XIII and IAA, Iodoacetamide. [a]The maximum number of exchangeable protons within the indicated peptide, assuming 100% deuteration. This value accounts for all exchangeable backbone amide protons and a slight fraction of N-terminal, C-terminal, and side chain exchangeable protons which are dependent on the final percentage of D_2O in solution under quench conditions (approximately 4.5%). A fully deuterated peptide would theoretically have acquired this amount of deuterons.

Table S2: Deuterium Incorporation for FXIII at Ten Minutes

Residues	Theo. D_{max} [a]	Zymogen	$FXIIIa^{Ca}$	K9 DON $FXIIIa^{Ca}$	IAA $FXIIIa^{Ca}$	$FXIIIa^{IIa}$	K9 DON $FXIIIa^{IIa}$	IAA $FXIIIa^{IIa}$
98-104	6.5	4.8 ± 0.1	3.8 ± 0.1	2.8 ± 0.1	2.5 ± 0.0	n/a	n/a	n/a
220-230	10.8	2.9 ± 0.1	3.9 ± 0.3	3.7 ± 0.1	3.6 ± 0.2	3.7 ± 0.0	3.6 ± 0.1	3.7 ± 0.1
240-247	7.5	1.4 ± 0.0	1.9 ± 0.1	1.8 ± 0.0	2.0 ± 0.1	1.9 ± 0.0	1.9 ± 0.1	2.1 ± 0.2
248-264	15.9	3.5 ± 0.0	n/a	n/a	n/a	4.0 ± 0.1	3.9 ± 0.0	n/a
513-522	9.7	3.9 ± 0.0	2.8 ± 0.1	2.7 ± 0.0	2.3 ± 0.2	3.3 ± 0.0	2.9 ± 0.3	2.9 ± 0.0
526-546	21.2	13.0 ± 0.1	7.5 ± 0.2	6.1 ± 0.3	n/a	12.5 ± 0.2	10.5 ± 0.8	11.0 ± 0.2
535-541	6.5	0.7 ± 0.0	0.8 ± 0.0	0.8 ± 0.0	0.9 ± 0.1	0.9 ± 0.0	1.0 ± 0.0	1.0 ± 0.1

FXIII, Factor XIII and IAA, Iodoacetamide. [a]The maximum number of exchangeable protons within the indicated peptide, assuming 100% deuteration. This value accounts for all exchangeable backbone amide protons and a slight fraction of N-terminal, C-terminal, and side chain exchangeable protons which are dependent on the final percentage of D_2O in solution under quench conditions (approximately 4.5%). A fully deuterated peptide would theoretically have acquired this amount of deuterons.

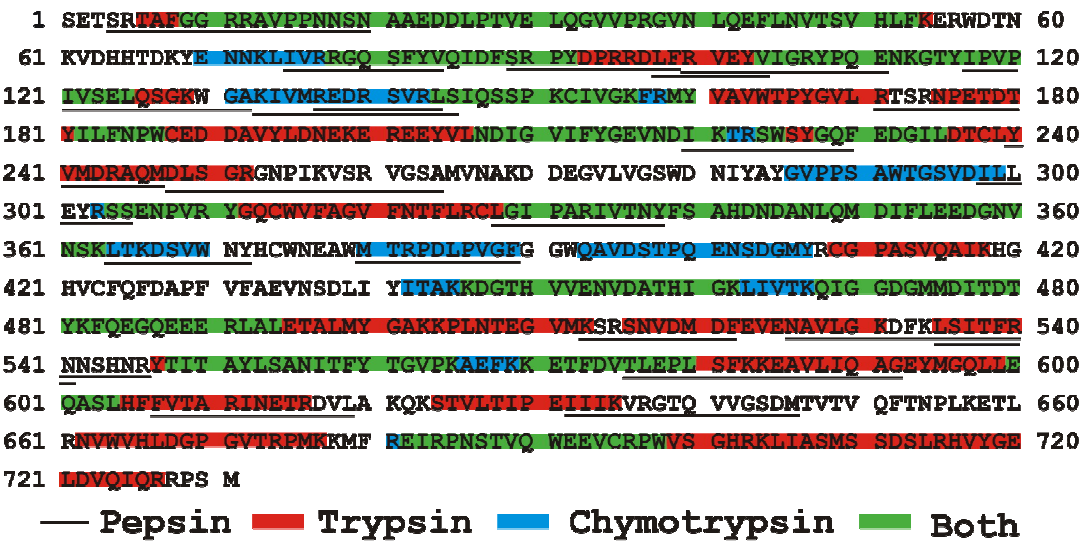

Figure S1: Sequence Coverage Map of FXIII. Pepsin fragments monitored during HDX experiments are underlined (45% sequence coverage) (*22*). Residues highlighted in red represent trypsin coverage (68%), in blue indicates chymotrypsin coverage (48%), and in green displays regions where the proteases overlap (81%).