

Table S1. Expected and observed peptide masses by MALDI-TOF MS.

Peptide	[M+H] ⁺ <i>m/z</i>			Expected	Observed
	Expected	Observed			
α -host	2223.1	2223.4	P5 β^3	2237.1	2236.8
P5Ala	2138.0	2137.6	P4 β^3	2237.1	2236.9
P4Ala	2195.1	2194.8	P3 β^3	2237.1	2236.8
P3Ala	2180.1	2179.9	P2 β^3	2237.1	2236.1
P1Ala	2131.1	2131.4	P1 β^3	2237.1	2237.1
P1'Ala	2166.1	2165.8	P1' β^3	2237.1	2237.4
P2'Ala	2207.1	2205.9	P2' β^3	2237.1	2237.0
P5D	2223.1	2221.2	P3' β^3	2237.1	2236.0
P4D	2223.1	2222.5	P5Aib	2152.1	2151.8
P3D	2223.1	2222.3	P4Aib	2209.1	2208.6
P2D	2223.1	2223.1	P3Aib	2194.1	2193.9
P1D	2223.1	2221.9	P2Aib	2237.1	2237.3
P1'D	2223.1	2223.5	P1Aib	2145.1	2143.6
P2'D	2223.1	2223.1	P1'Aib	2180.1	2179.6
P3'D	2223.1	2221.5	P2'Aib	2221.1	2220.8
P5N-Me	2237.1	2236.8	P3'Aib	2237.1	2236.6
P4N-Me	2237.1	2236.3	P2-P2' β^3	2251.1	2249.4
P3N-Me	2237.1	2236.7	P3-P2' β^3	2251.1	2250.1
P2N-Me	2237.1	2237.5	P4-P2' β^3	2251.1	2250.9
P1N-Me	2237.1	2236.6	P4-P3' β^3	2251.1	2250.0
P1'N-Me	2237.1	2237.4	P5-P3' β^3	2251.1	2250.6
P2'N-Me	2237.1	2236.4	P4-P3'D	2223.1	2223.1
P3'N-Me	2237.1	2237.0	P4-P3'N-Me	2251.1	2250.9
			P4-P3'Aib	2223.1	2222.7

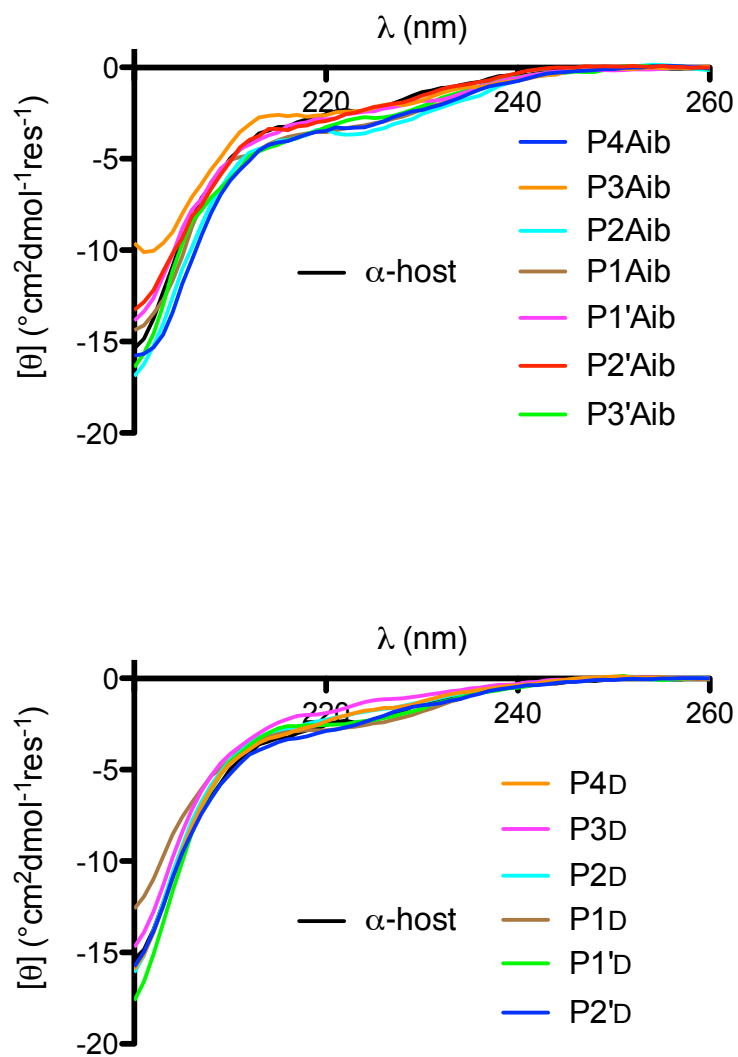


Figure S1. Circular dichroism (CD) scan spectra of α -host peptide compared with Aib (top) and D-residue (bottom) substituted peptides.

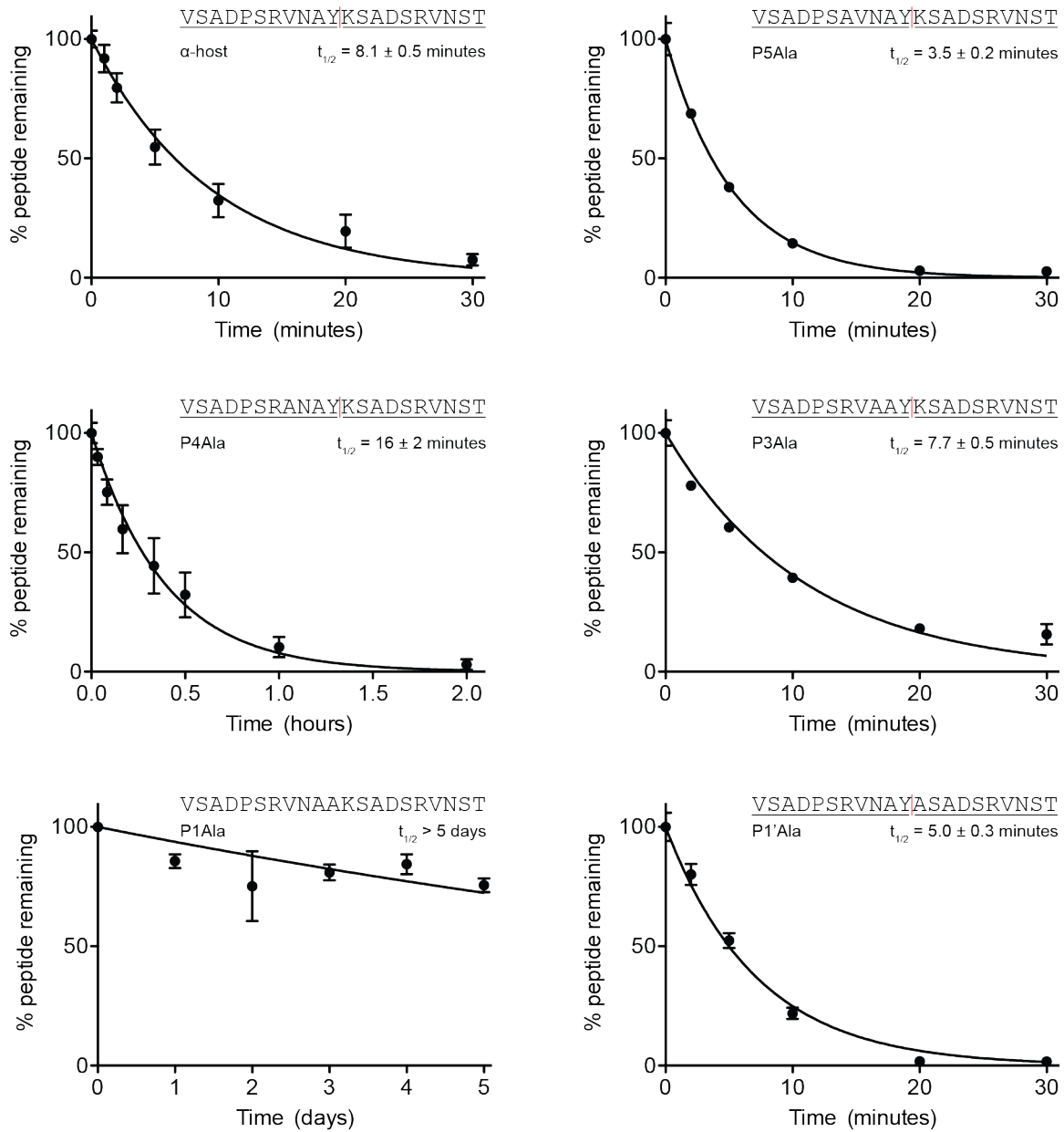


Figure S2. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_p) e^{-kx} + Y_p$ (solid curve).

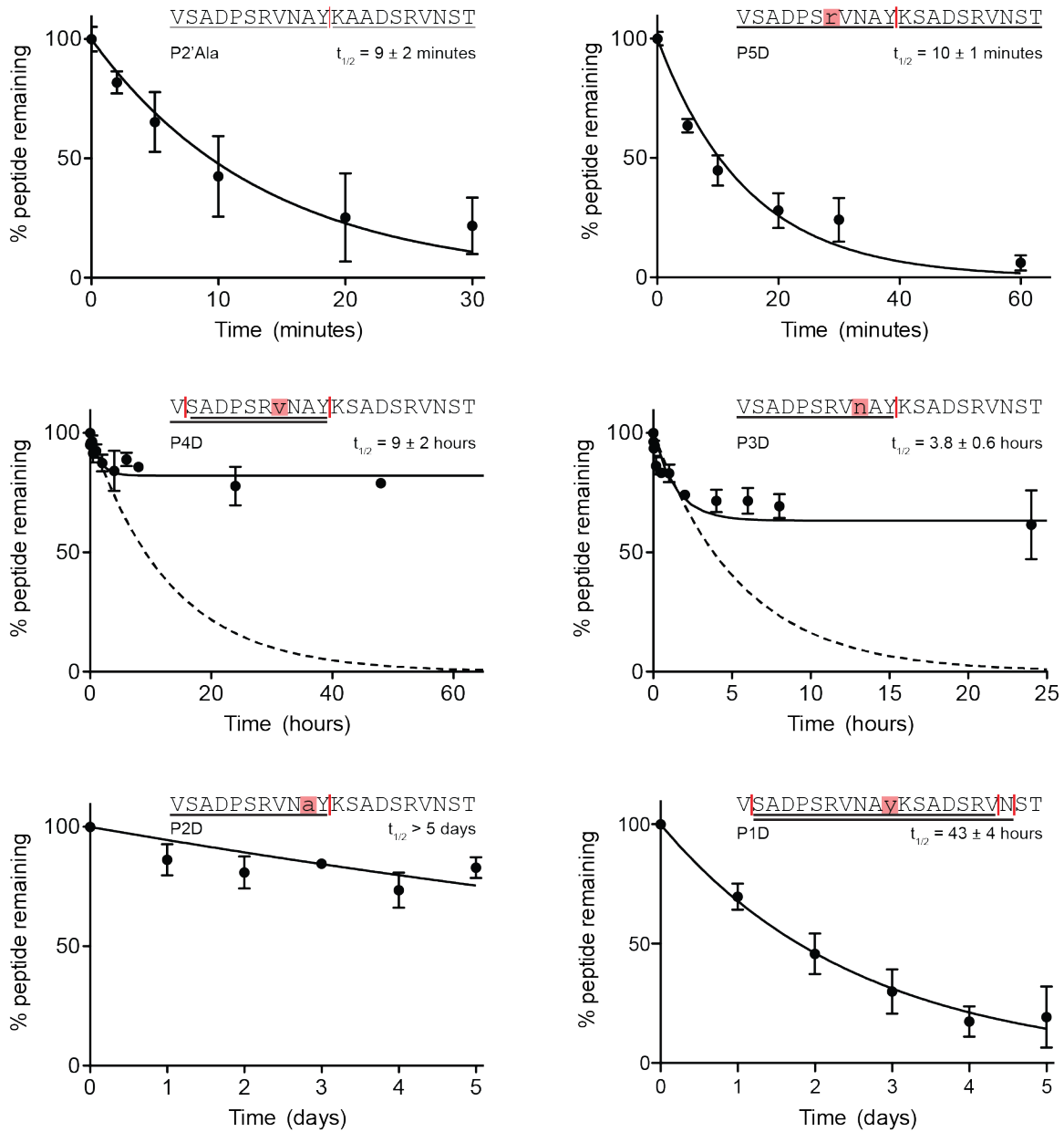


Figure S3. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_p) e^{-kx} + Y_p$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).

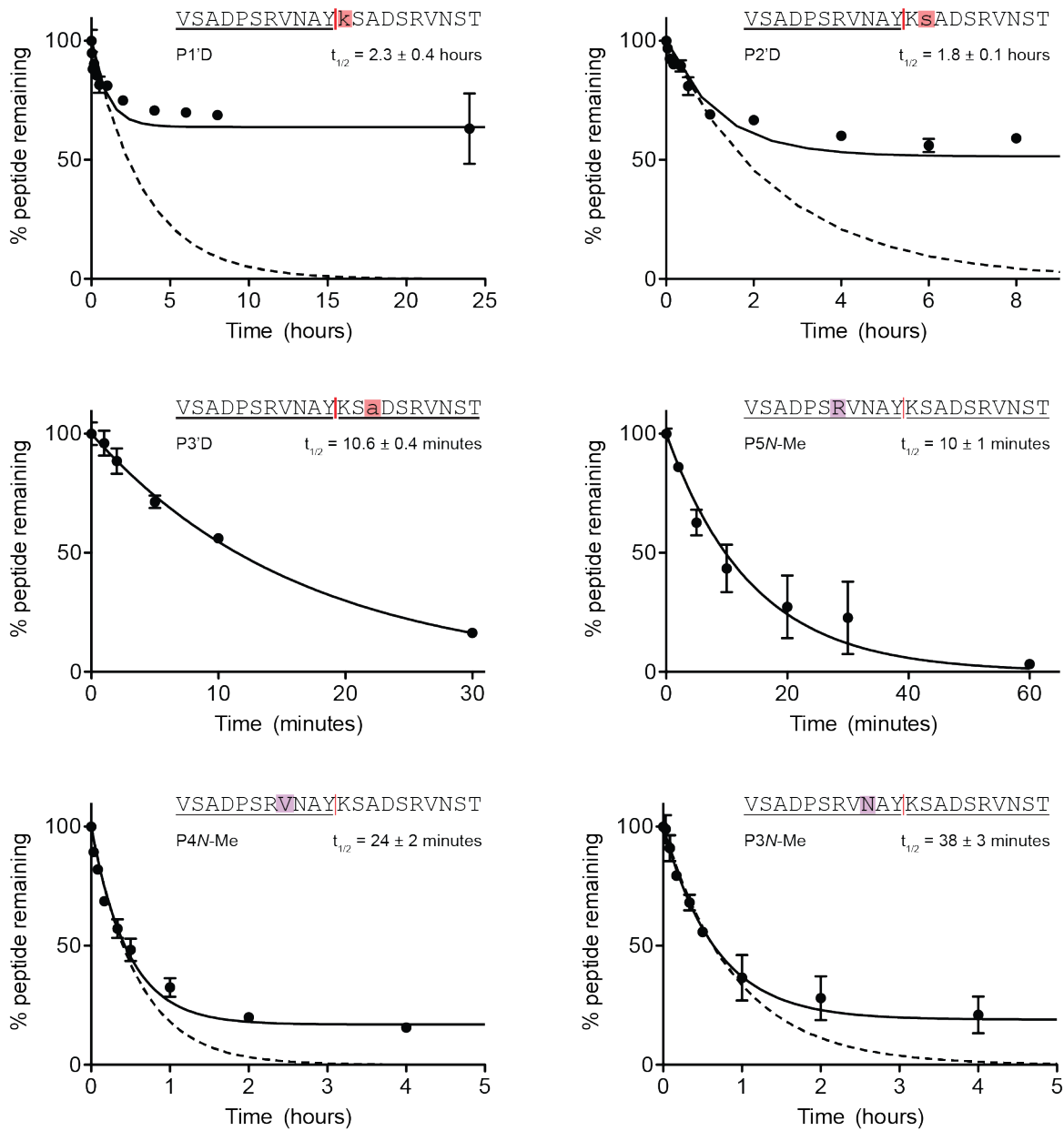


Figure S4. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_p) e^{-kx} + Y_p$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).

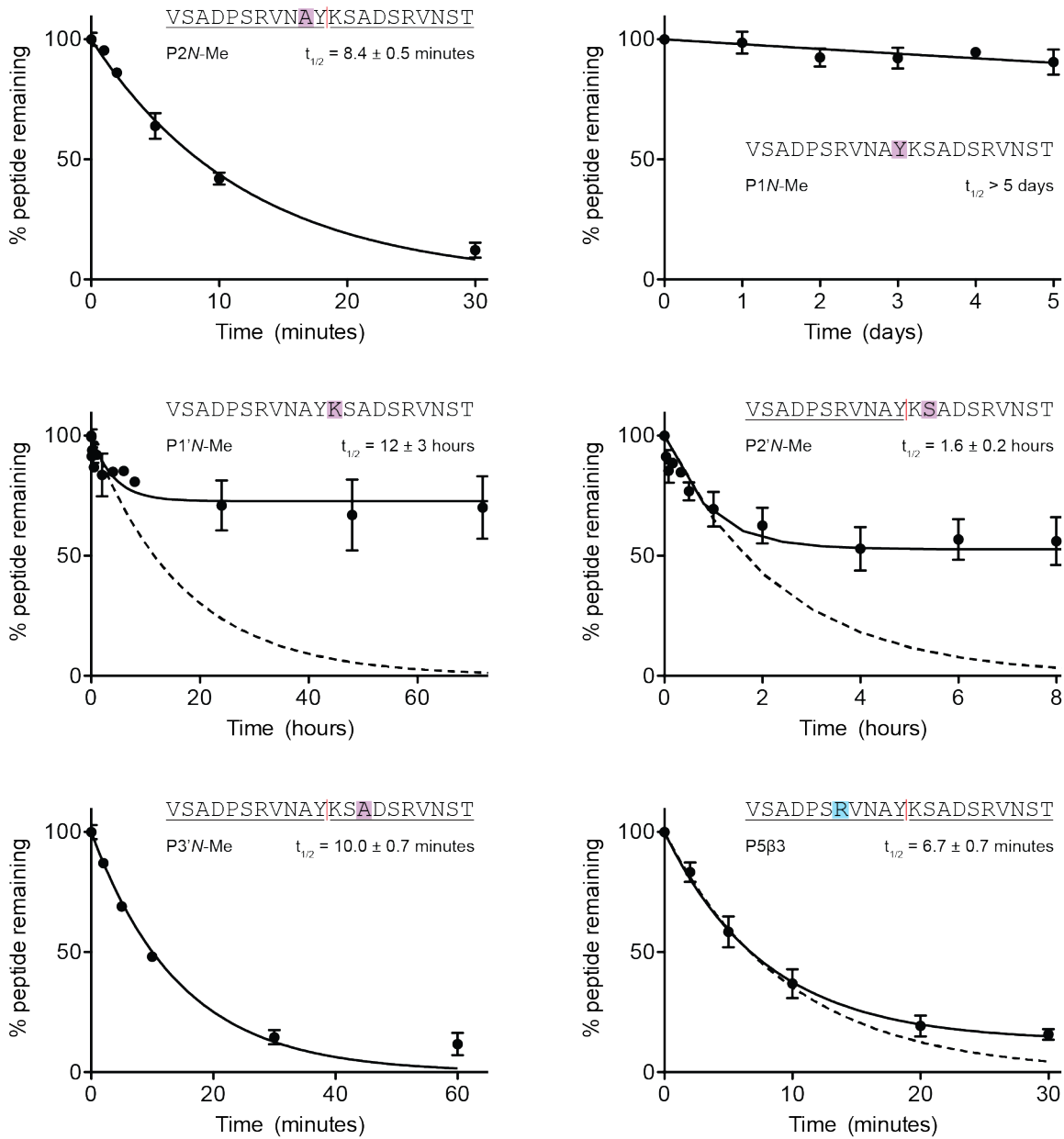


Figure S5. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_p) e^{-kx} + Y_p$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).

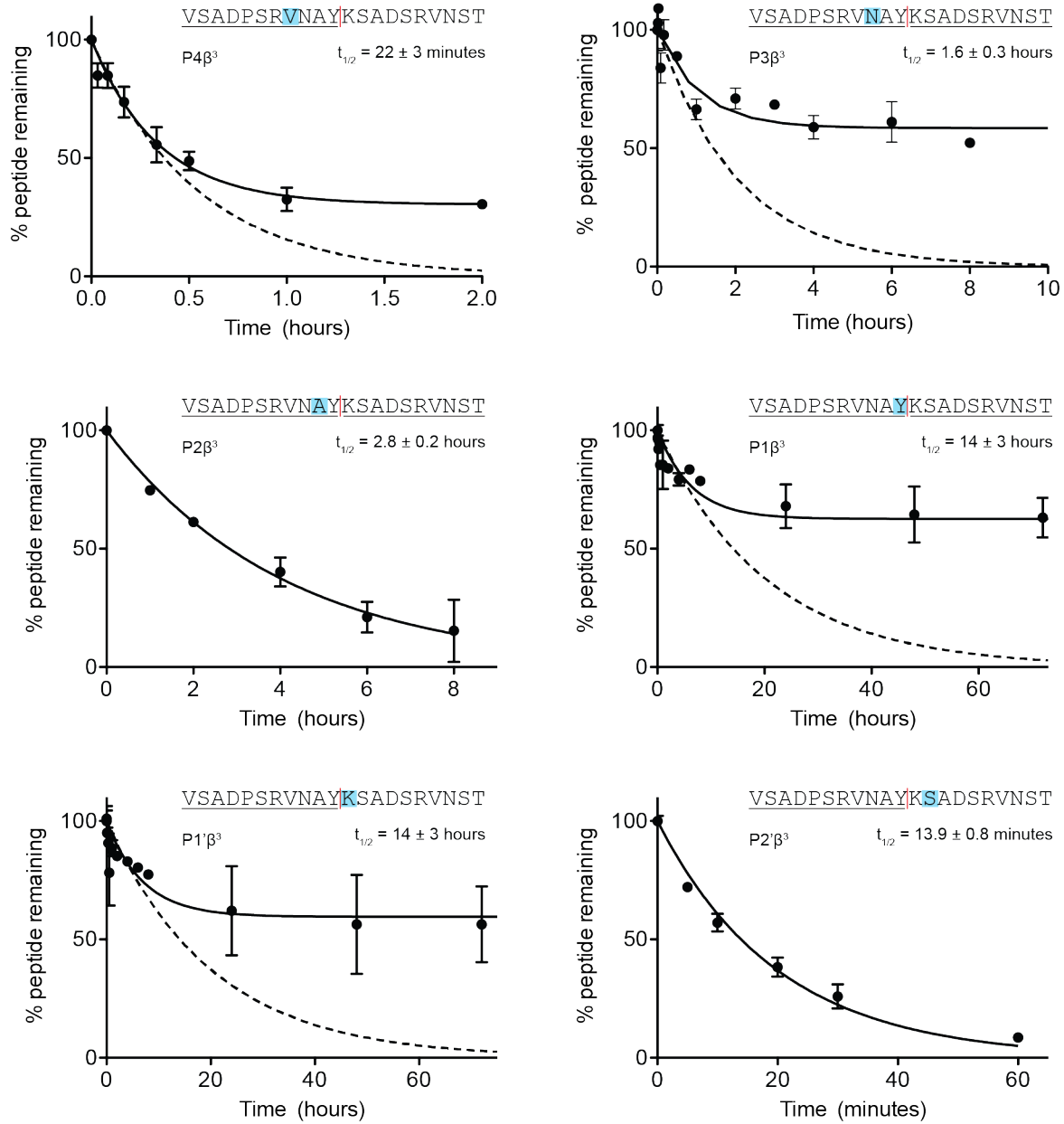


Figure S6. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_P) e^{-kx} + Y_P$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).

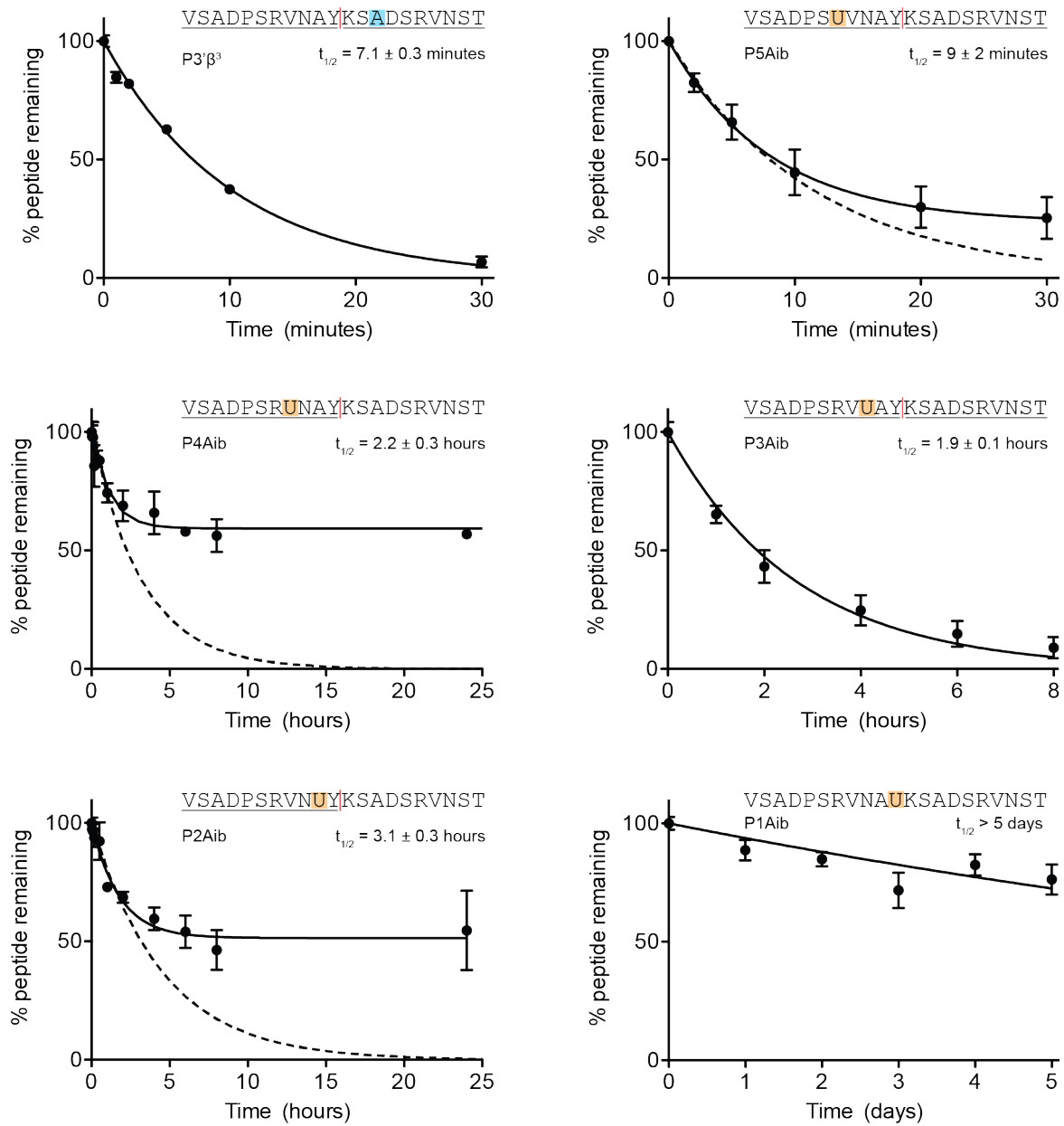


Figure S7. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_P) e^{-kx} + Y_P$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).

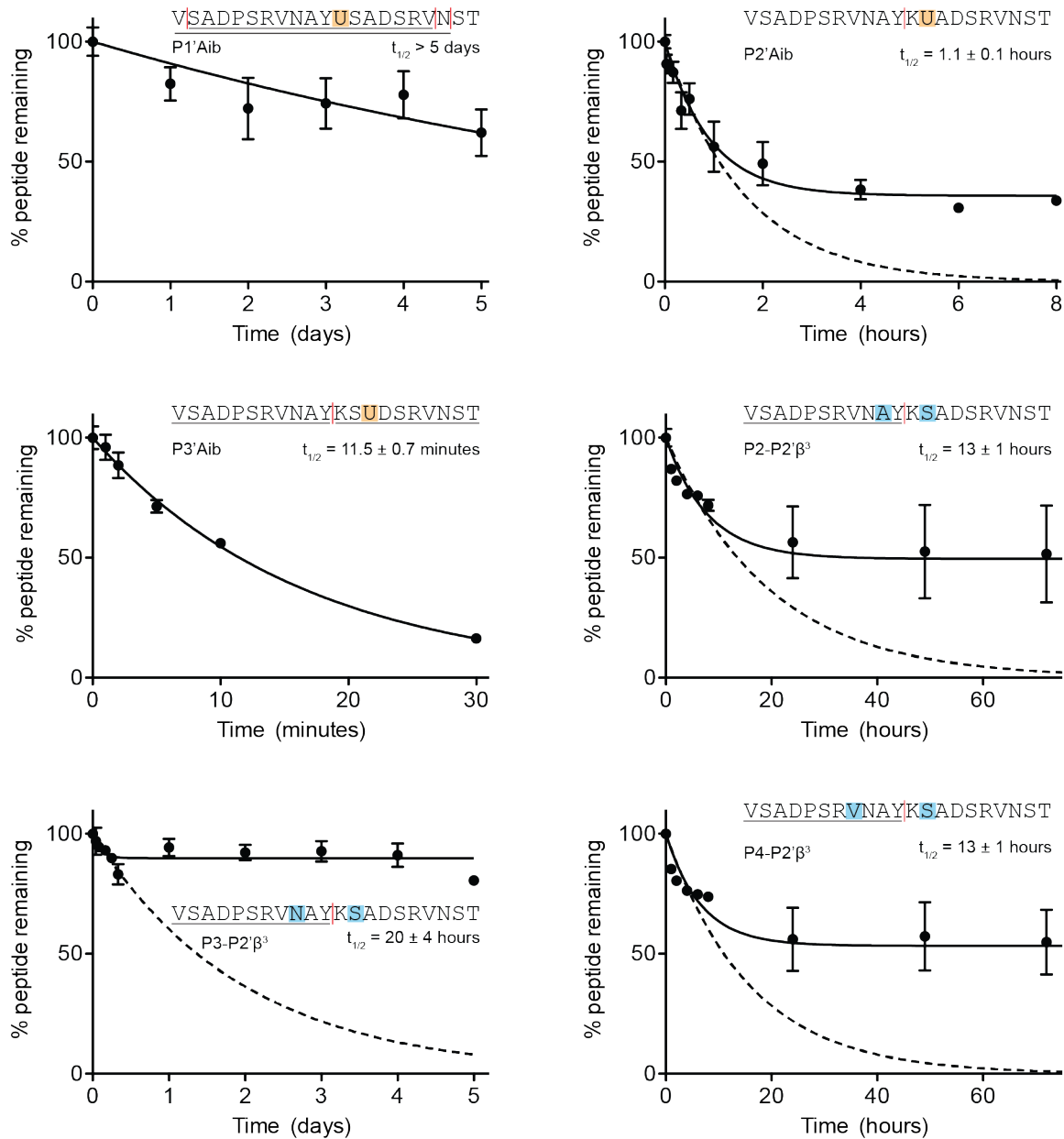


Figure S8. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_p) e^{-kx} + Y_p$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).

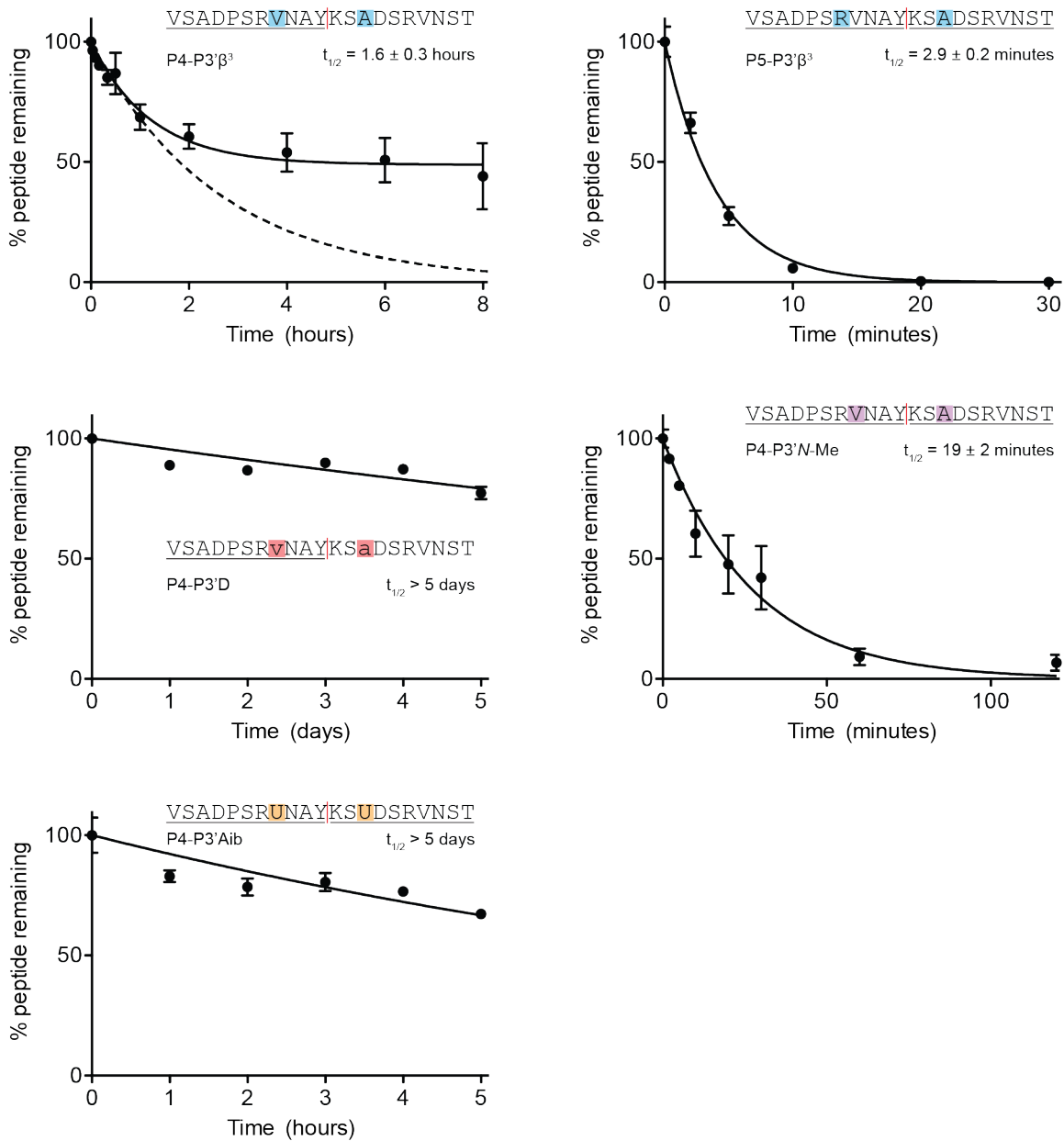


Figure S9. Full progress degradation curves and calculated half-lives of various peptides. Observed proteolysis products (horizontal black lines) and corresponding cleavage sites (vertical red lines) for each peptide are indicated in its sequence. Data points represent at least two replicate proteolysis experiments and are modeled by a one-phase decay fit with a variable plateau value $Y = (Y_0 - Y_P) e^{-kx} + Y_P$ (solid curve). For peptides that did not degrade fully, the earliest data points are modeled by a one-phase decay model with a plateau constrained to zero $Y = (Y_0) e^{-kx}$ (hashed curve).