SUPPORTING INFORMATION

Residue-Based Preorganization of BH3-Derived α/β-Peptides: Modulating Affinity, Selectivity and Proteolytic Susceptibility in α-Helix Mimics

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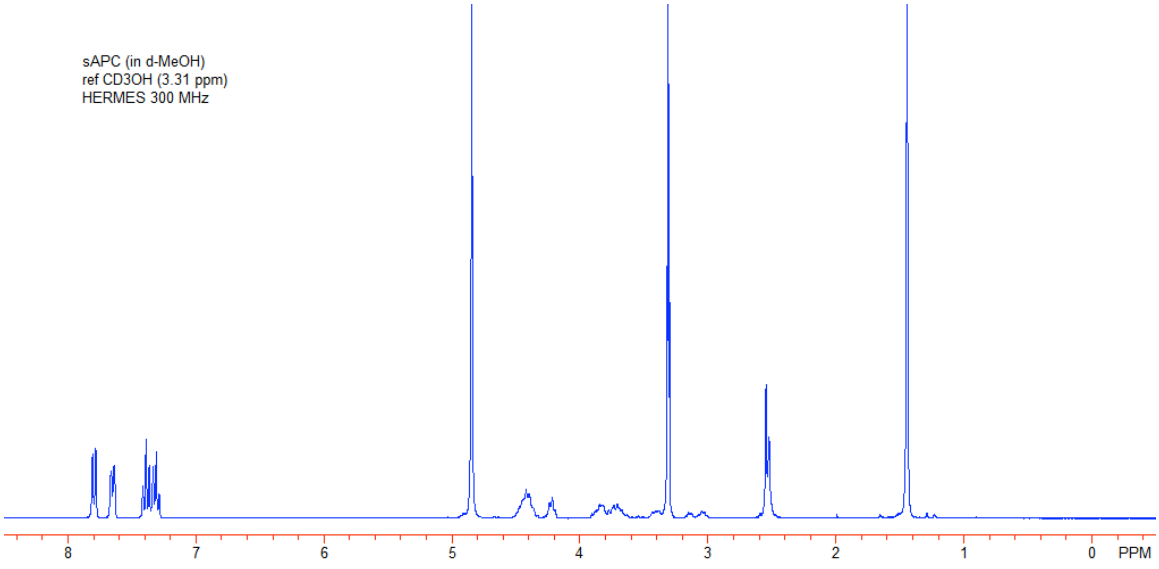
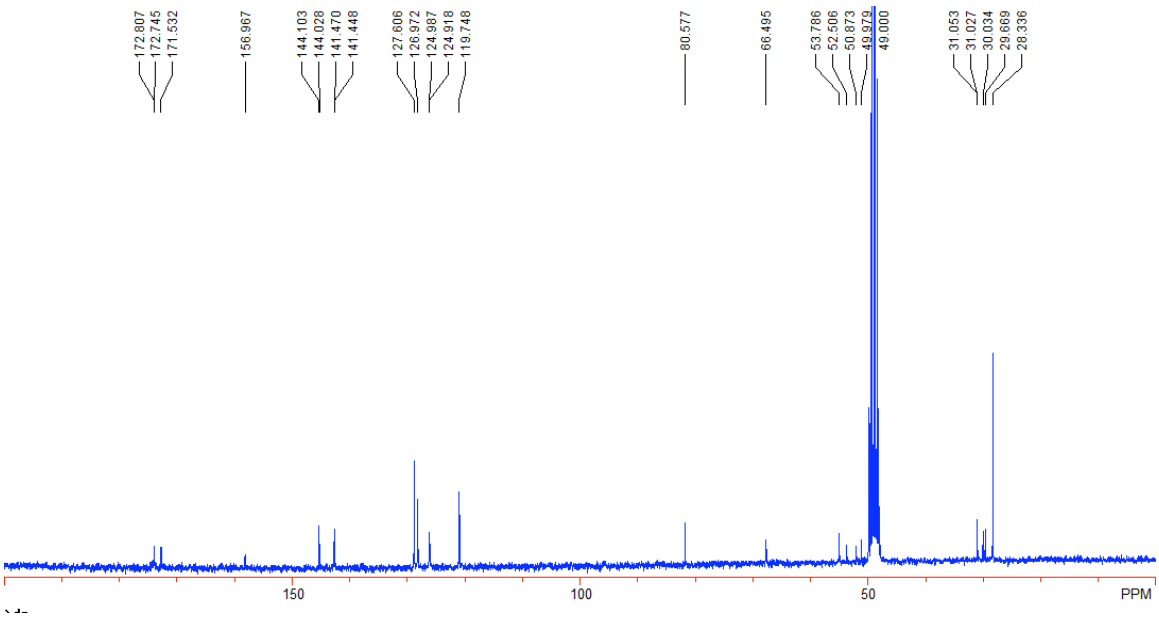
NMR data. Shown below are ^{1}H NMR and ^{13}C NMR data for protected β-amino acid **1**.





Representative competition fluorescence polarization assay data. These studies were conducted as described in the main text.

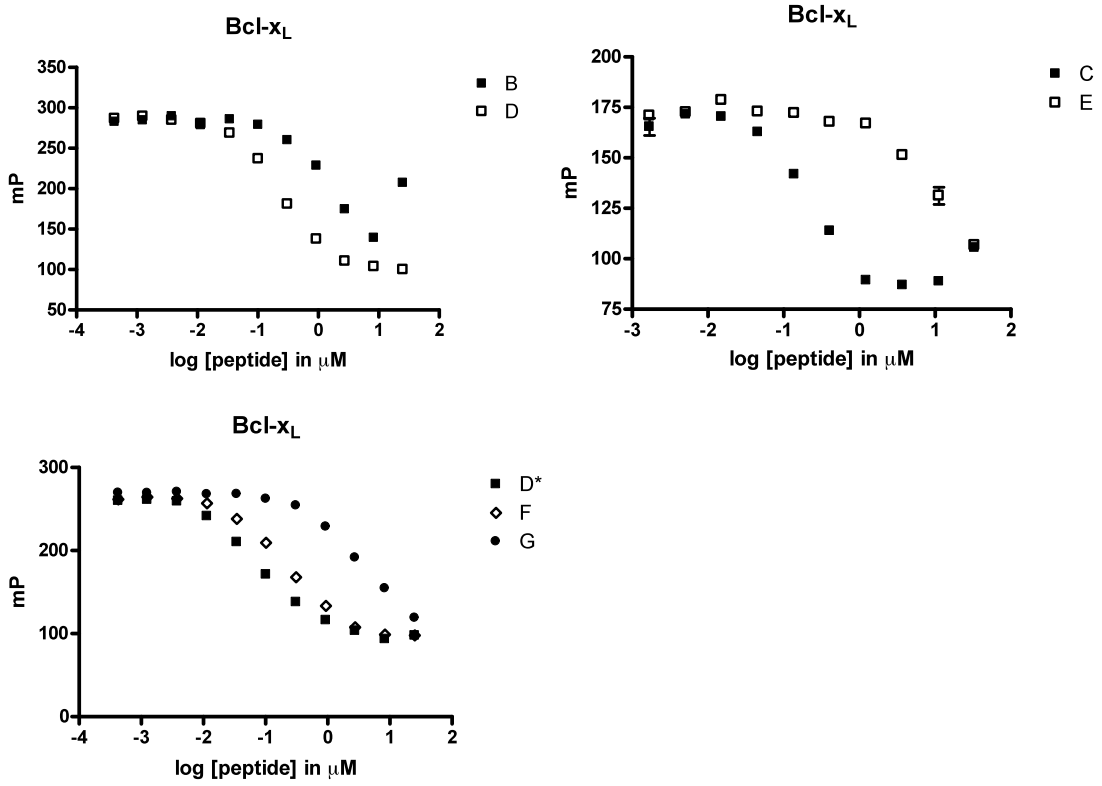


Figure S1. Representative competition fluorescence polarization (FP) data for α/β-peptides **B**, **C**, **D**, **D***, **E**, **F**, and **G** binding to Bcl-x_L.

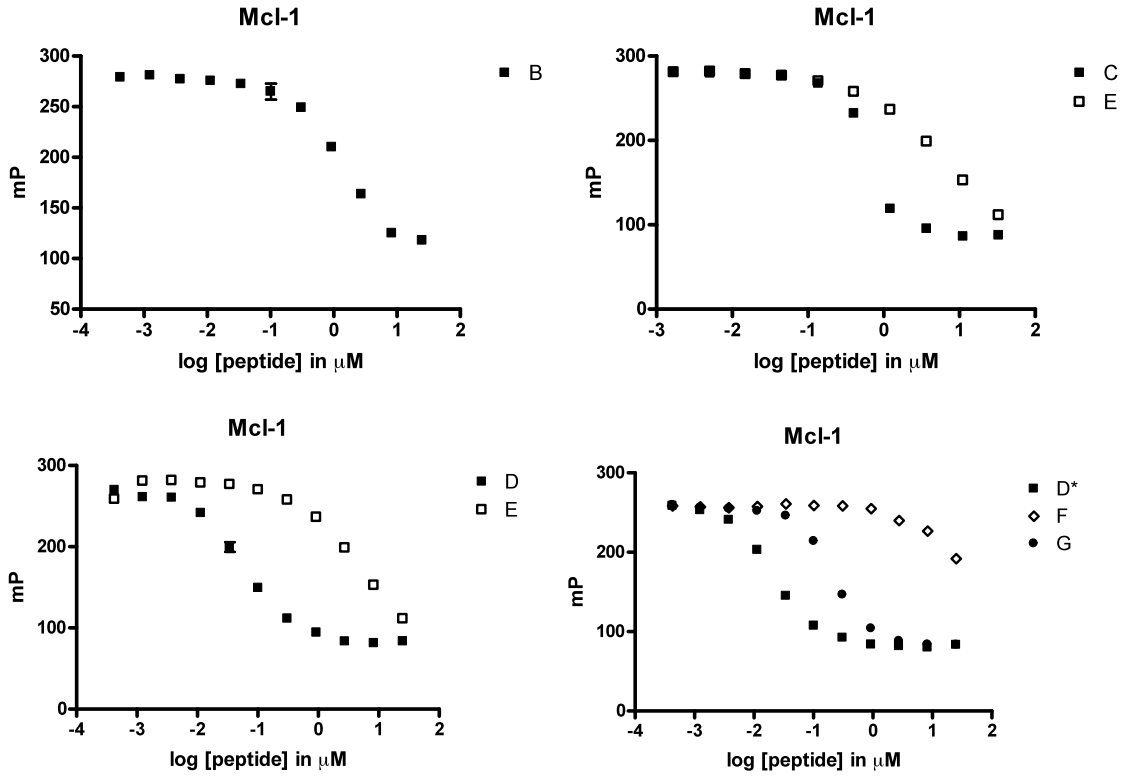
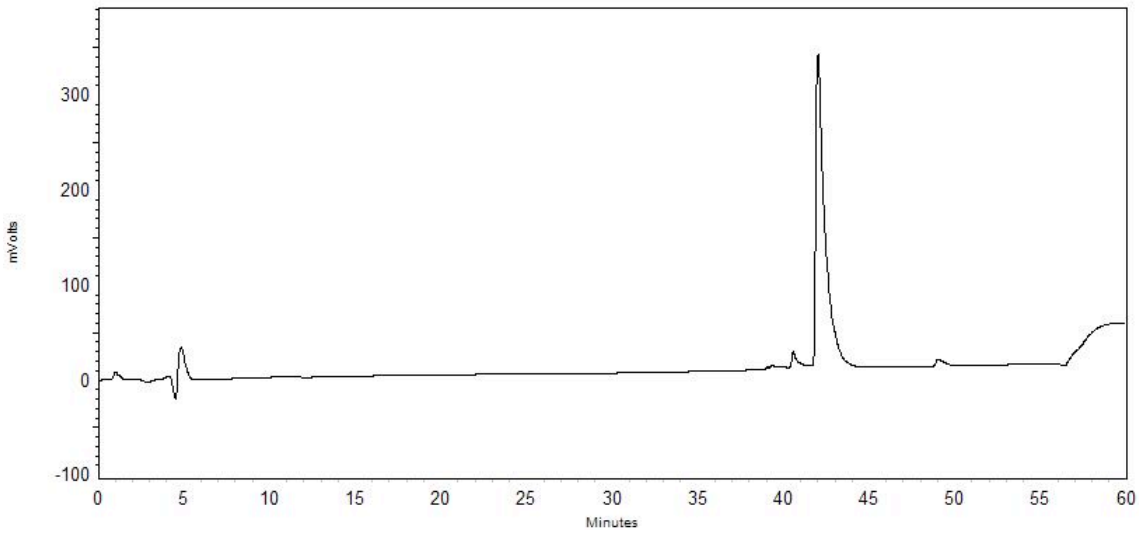


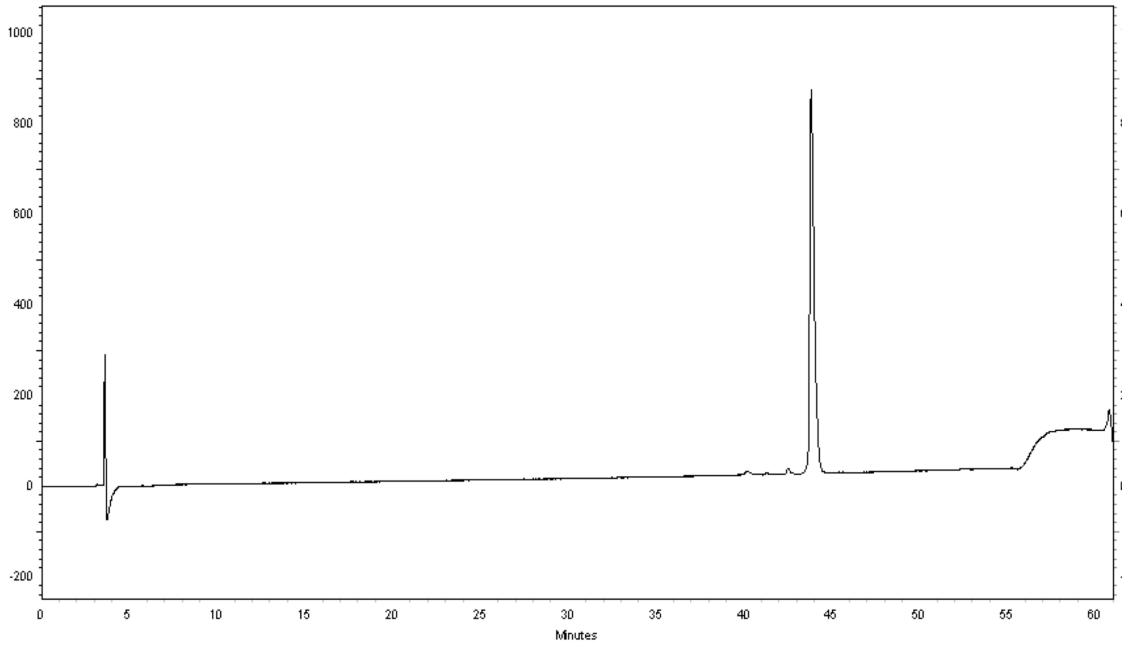
Figure S2. Representative competition fluorescence polarization (FP) data for α/β-peptides **B**, **C**, **D**, **D***, **E**, **F**, and **G** binding to Mcl-1.

Peptide Characterization. Following lyophilization, peptide purity was assessed through HPLC and MALDI-TOF analyses. Analytical HPLC was run on a C4 or C18 analytical column using a 10-60% MeCN + 0.1% TFA (B solvent) in water + 0.1% TFA (A solvent) over 50 minutes. The traces shown are based on UV absorbance at 220 nm (**Figure S3**). All peptides used in this study were ≥ 95% pure. Peptide identity was monitored by MALDI-TOF mass spectrometry (**Table S1**).

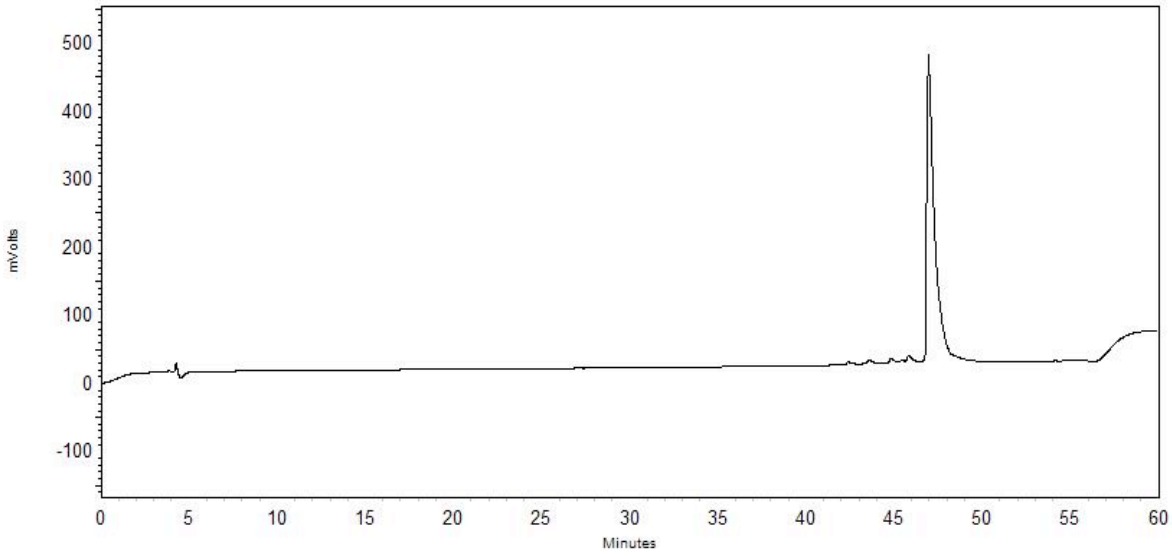
A



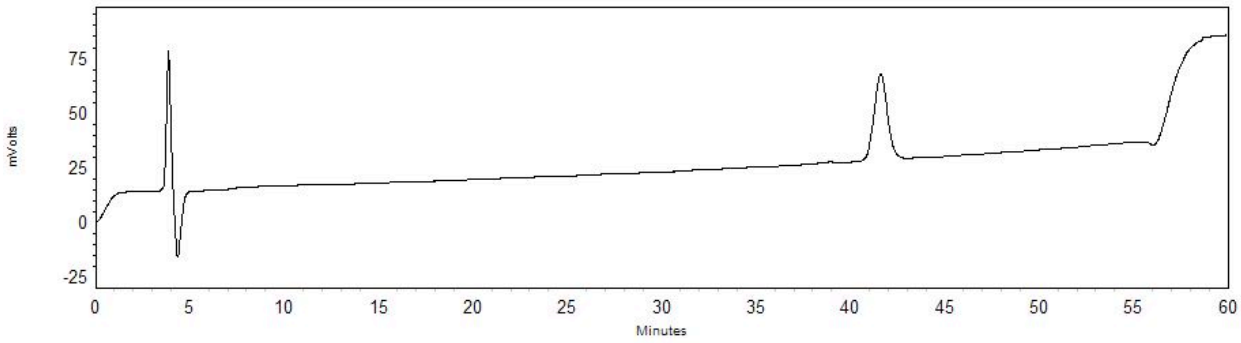
B



C



D



D*

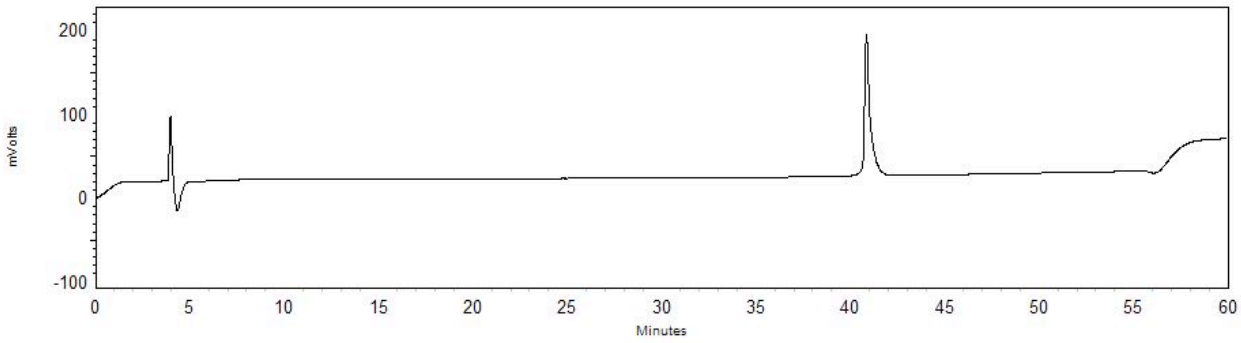


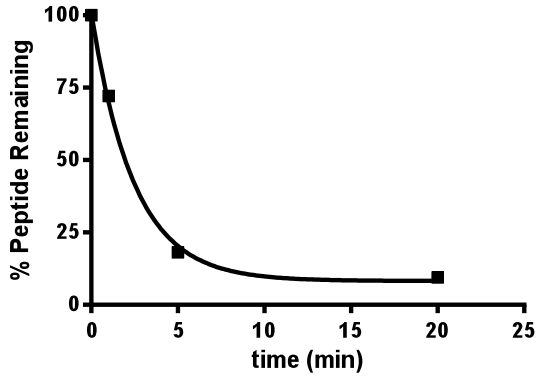
Figure S3. Analytical HPLC Traces for α-peptide **A** and α/β-peptides **B**, **C**, **D**, **D***, **E**, **F**, and **G**.

	$[M+H]^+$ expected	$[M+H]^+$ observed
A	2298.1	2297.8
B	2368.2	2367.5
C	2368.2	2368.0
D	2385.2	2384.9
D*	2351.2	2351.1
E	2216.2	2215.6
F	2266.2	2266.3
G	2232.2	2232.4

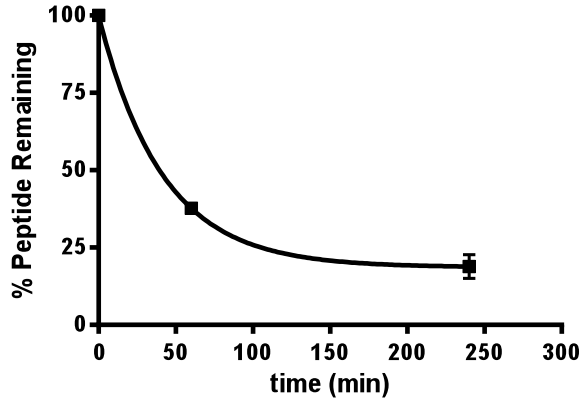
Table S1. Expected and observed masses of α-peptide **A** and α/β-peptides **B**, **C**, **D**, **D***, **E**, **F**, and **G** by MALDI-TOF-MS.

Proteolysis. These studies were carried out as described in the main text.

A)



B)



C)

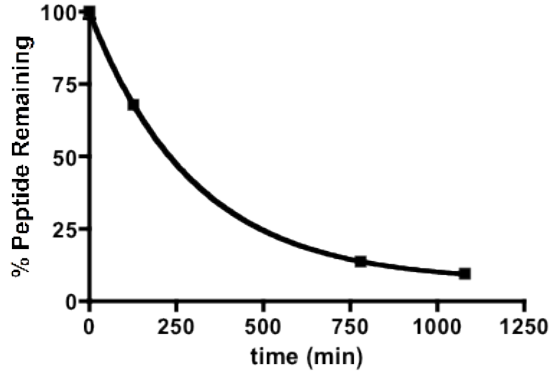


Figure S4. Curves resulting from proteolysis of 50 μM solutions of α-peptide **A** (A) or α/β-peptide **B** (B) or **D** (C), in the presence of 10 mg/mL proteinase K as a function of time. Reactions were run in TBS buffer, pH 7.5, with 5% DMSO, and quenched with 1% TFA in 50:50 acetonitrile:H_2O. Curves result from fitting the data to an exponential decay model in GraphPad Prism. Note the substantial differences in x-axes among the graphs.