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## **Supporting Information**

Design, Synthesis and Characterization of A Potent, Non-Peptide, Cell-Permeable, Bivalent  
Smac Mimetic that Concurrently Targets both the BIR2 and BIR3 Domains in XIAP

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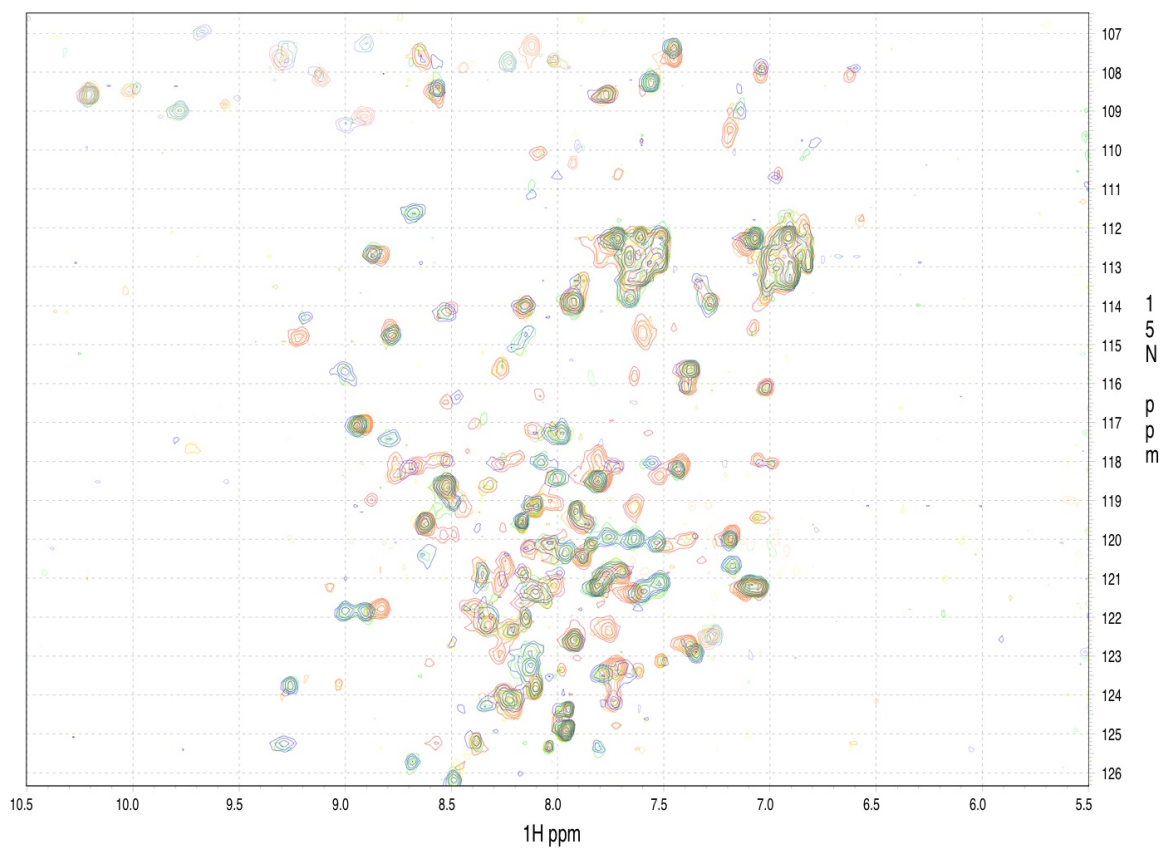
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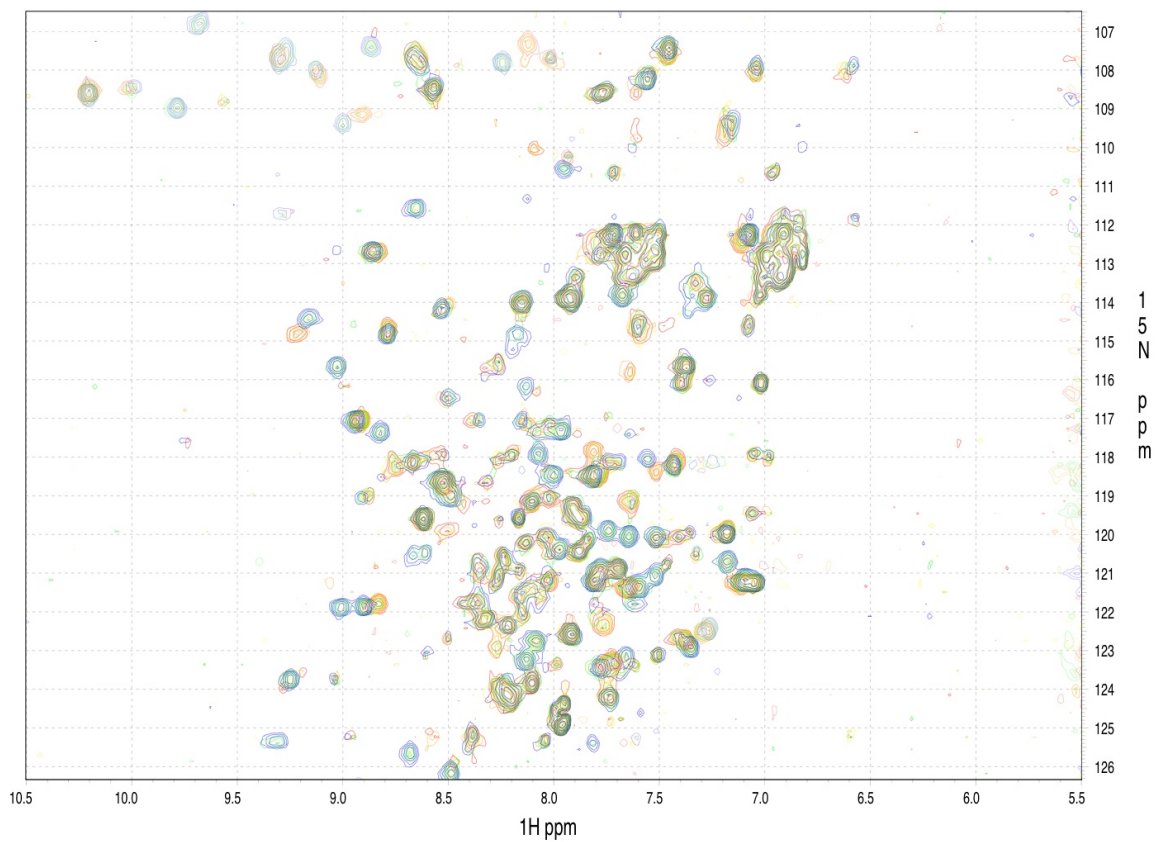
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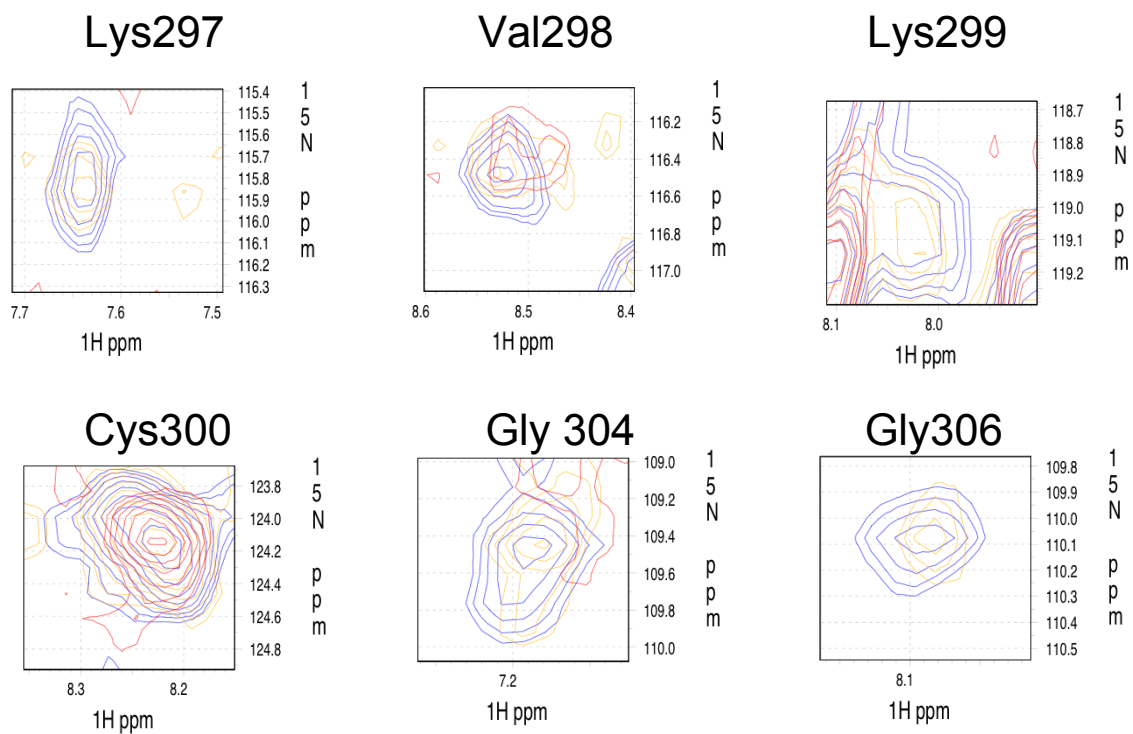
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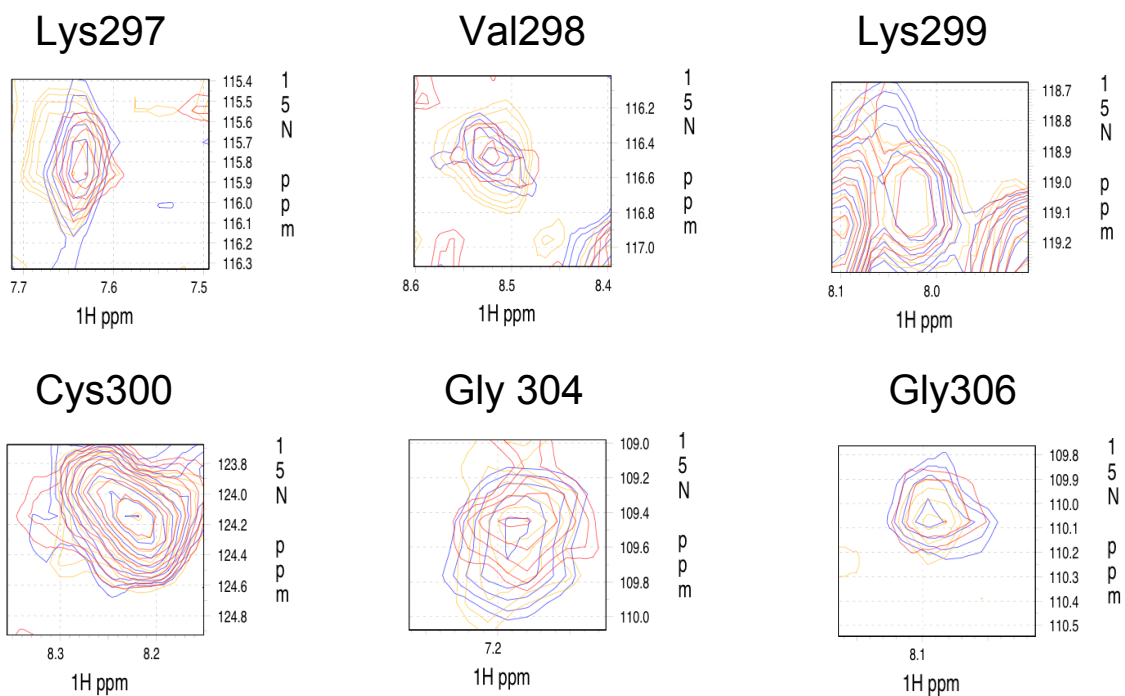
**Figure S1.** <sup>15</sup>N-HSQC NMR spectra of XIAP BIR2-BIR3 protein at 100 μM with different concentrations of SM-164 (compound **4**) (red: 0; orange: 10; yellow: 30; green: 60; blue 150 μM).



**Figure S2.**  $^{15}\text{N}$ -HSQC NMR spectra of XIAP BIR2-BIR3 protein at 100  $\mu\text{M}$  with different concentrations of SM-122 (compound **1**) (red: 0; orange: 10; yellow: 30; green: 60; blue 150  $\mu\text{M}$ ).



**Figure S3.**  $^{15}\text{N}$ -HSQC NMR spectra of several BIR3 residues in XIAP BIR2-BIR3 protein (100  $\mu\text{M}$ ) with different concentrations of SM-164 (red: 0; orange: 10; yellow: 30; green: 60; blue 150  $\mu\text{M}$ ).



**Figure S4.**  $^{15}\text{N}$ -HSQC NMR spectra of several BIR3 residues in XIAP BIR2-BIR3 protein (100  $\mu\text{M}$ ) with different concentrations of SM-122 (red: 0; orange: 10; yellow: 30; green: 60; blue 150  $\mu\text{M}$ ).