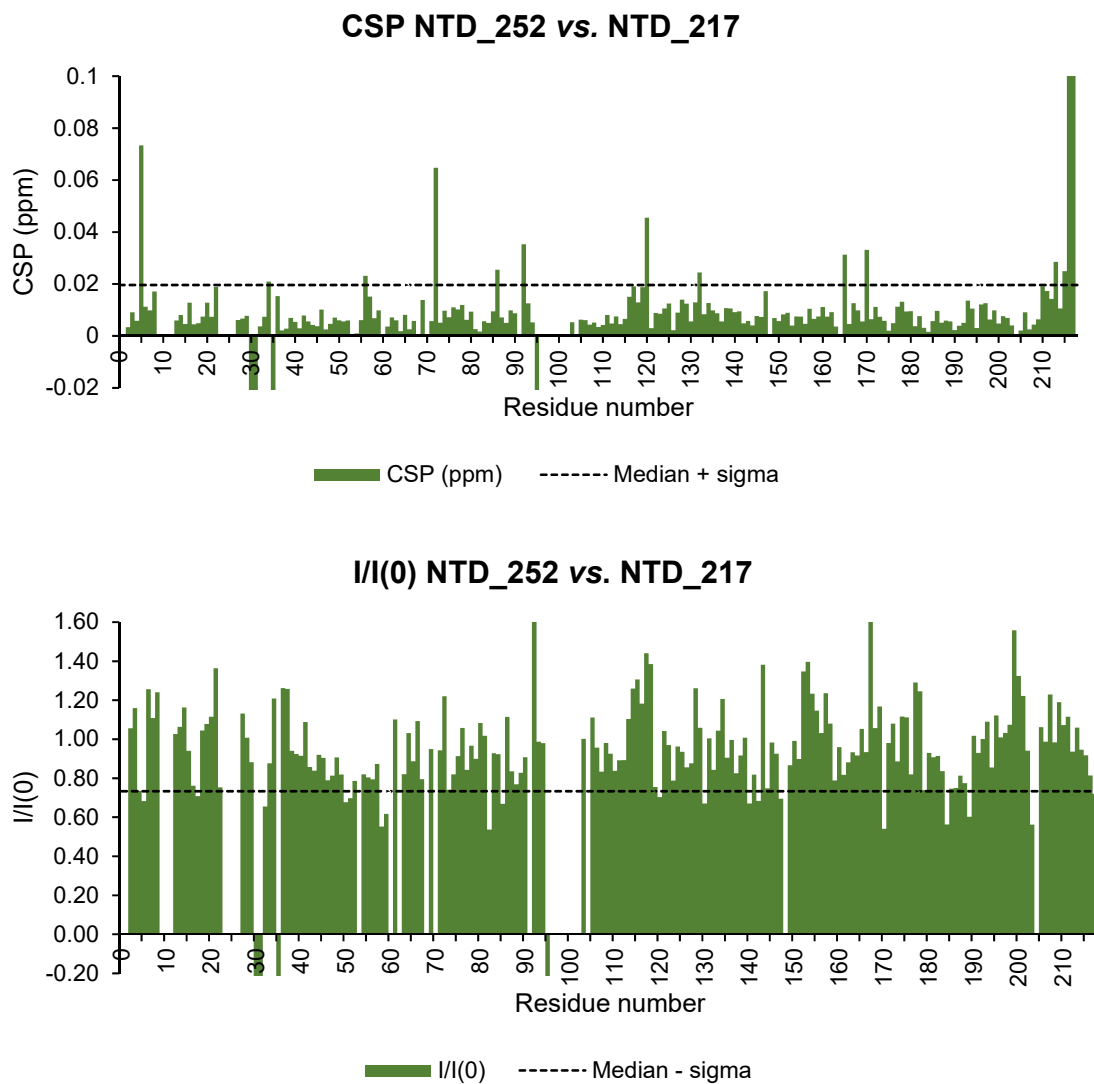


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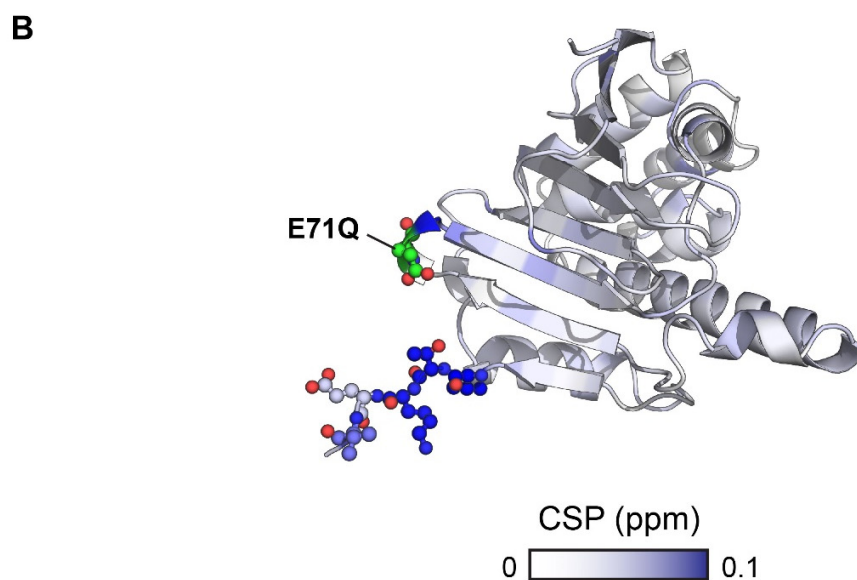
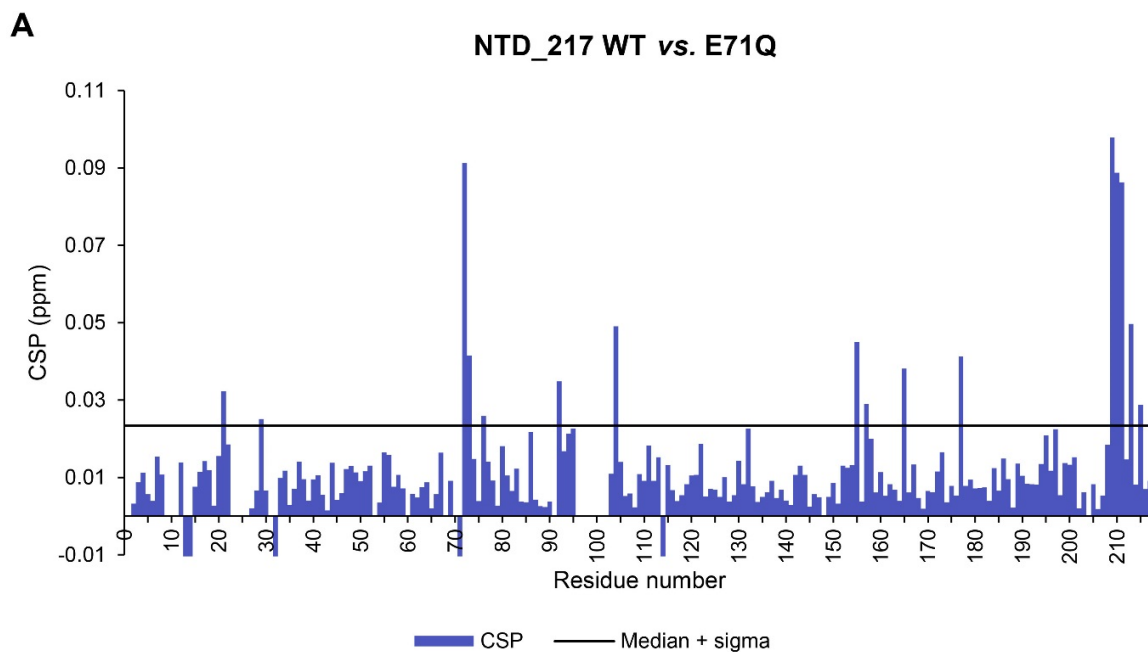
Supporting Information

## **The Charged Linker Modulates the Conformations and Molecular Interactions of Hsp90**

Abraham López, Annika R. Elimelech, Karolin Klimm, and Michael Sattler\*

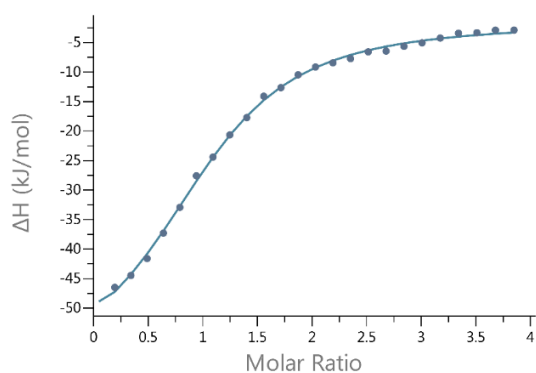
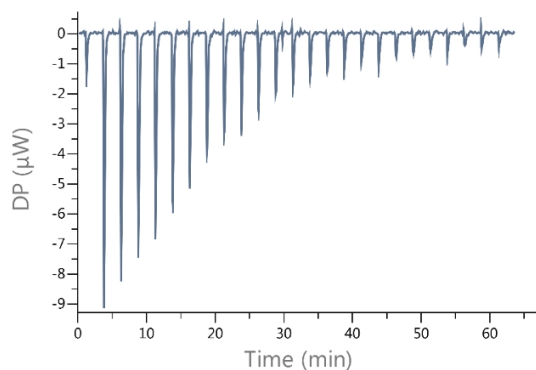


**Figure S1.** Comparison of NMR spectra of Hsp90 NTD constructs. The absence of significant CSP and intensity changes on the NTD between NTD\_252 and NTD\_217 indicates that only C-linker is responsible for interactions with N-linker and NTD.

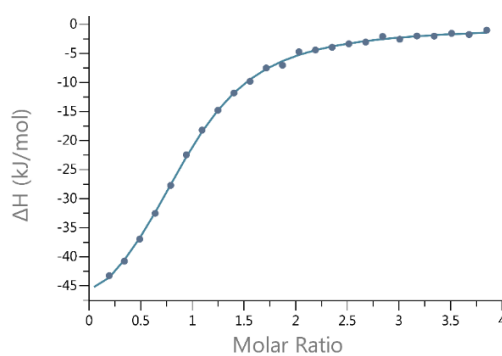
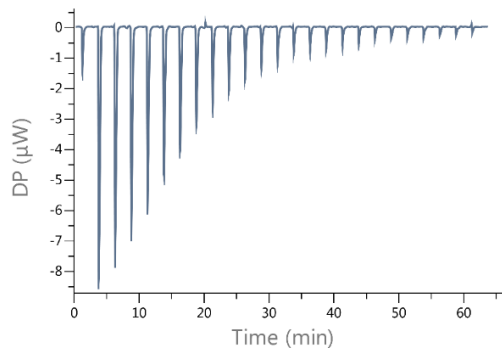


**Figure S2.** The  $\beta$ 2-  $\beta$ 3 turn stabilizes the N-linker region. A) CSPs of NTD\_217 WT vs. E71Q shows strong perturbations on N-linker residues 209-213, indicating a charge-mediated interaction. B) Mapping of perturbations derived from E71Q mutation (green) on crystal structure of NTD bound to ATP (PDB 1AM1<sup>[1]</sup>). Side chains of affected residues 209-215 are shown as sticks and spheres.

NTD\_217 + ADP



NTD\_274 + ADP



	$K_D$ ( $\mu\text{M}$ )	stoichiometry	$\Delta H$ (kJ/mol)	$\Delta G$ (kJ/mol)	$-T^*\Delta S$ (kJ/mol)
NTD_217 ADP	$20.7 \pm 1.91$	$1.04 \pm 0.017$	$-60.2 \pm 2.21$	-26.8	33.5
NTD_274 ADP	$14.9 \pm 0.82$	$0.912 \pm 0.009$	$-54.8 \pm 1.05$	-27.6	27.3

**Figure S3:** Summary of isothermal titration calorimetry experiments for nucleotide binding to NTD-linker constructs.

**Supplementary References**

- [1] C. Prodromou, S. M. Roe, R. O'Brien, J. E. Ladbury, P. W. Piper, L. H. Pearl, *Cell* **1997**, *90*, 65-75.