Supporting Information

Solution Observation of Dimerization and Helix Handedness Induction in a Human Carbonic Anhydrase–Helical Aromatic Amide Foldamer Complex

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Supporting Information

Figure S1  NMR spectra of HCA in TRIS and phosphate
Figure S2  NMR spectra of HCA-3 in TRIS and phosphate compared to HCA
Figure S3  Intermolecular contacts in phosphate for HCA and HCA-1 identified by NMR spectroscopy
Figure S4  NMR spectra of HCA-1 in TRIS and phosphate compared to HCA-3
Figure S5  NMR spectra of HCA-2 in TRIS and phosphate compared to HCA-3
Figure S6  Intermolecular contacts in phosphate for HCA-2 identified by NMR spectroscopy
Figure S7  Analysis of compound 2 by HPLC and ESI-MS
Figure S8  Analysis of compound 2 by $^1$H NMR
Figure S1. NMR spectra of HCA in TRIS and phosphate. A) $^1$H,$^{15}$N TROSY of 300 μM [$^{15}$N]-HCA in 50 mM TRIS pH 7.4. B) $^1$H,$^{15}$N-HSQC of 500 μM [$^{15}$N]-HCA in 50 mM sodium phosphate pH 7.4. In both spectra the backbone amide crosspeaks are annotated with residue type and sequence number.
Figure S2. NMR spectra of HCA-3 in TRIS and phosphate compared to HCA. A) $^1$H, $^{15}$N TROSY of 300 μM [$^{15}$N]-HCA in 50 mM TRIS pH 8.0 without (black) and with (blue) 1.3 molar equivalents of compound 3. B) $^1$H, $^{15}$N-HSQC of 500 μM [$^{15}$N]-HCA in 50 mM sodium phosphate pH 7.4 without (black) and with (blue) 1.3 molar equivalents of compound 3.
Figure S3. Intermolecular contacts in phosphate for HCA and HCA-1 identified by NMR spectroscopy. A) Region of $^1$H, $^{15}$N-HSQC spectra (Figure S2B) from samples of unbound 300 μM $^{15}$N-HCA in phosphate without (black) and with (blue) 1.3 molar equivalents of added compound 3. Selected crosspeaks have been annotated. B) $\Delta \delta_{HN}$ of HCA-3 compared to HCA, calculated as the root mean square deviation, $((\Delta \delta_H/0.14)^2+(\Delta \delta_N)^2)^{0.5}$. C) Each observed amide nitrogen atom in the $^1$H, $^{15}$N-HSQC is represented as a sphere on the structure of HCA (chain A from PDB ID 4LP6) and colored as in (B). The top orientation is the same as the green HCA protein in Figure 1A. D) Region of $^1$H, $^{15}$N-TROSY spectra overlay (Figure S4B) of HCA-1 (red) and the $^1$H$^{15}$N-HSQC of HCA-3 (blue) in phosphate buffer. E) $\Delta \delta_{HN}$ of HCA-1 compared to HCA-3, calculated as in (B). F) Each observed amide is represented as a sphere on the structure of HCA and colored as in (E).
**Figure S4**  NMR spectra of HCA-1 in TRIS and phosphate compared to HCA-3. A) $^1$H,$^{15}$N TROSY of 300 μM $[^{15}$N]-HCA in 50 mM TRIS pH 8.0 with 1.3 molar equivalents of compound 1 (red) or compound 3 (blue). B) $^1$H,$^{15}$N-HSQC of 270 μM $[^{15}$N]-HCA in 50 mM sodium phosphate pH 7.4 with 1.3 molar equivalents of compound 1 (red) or compound 3 (blue).
Figure S5. NMR spectra of HCA-2 in TRIS and phosphate compared to HCA-3. A) $^1$H,$^{15}$N TROSY of 300 μM [$^{15}$N]-HCA in 50 mM TRIS pH 8.0 with 1.3 molar equivalents of compound 2 (green) or compound 3 (blue). B) $^1$H,$^{15}$N-HSQC of 500 μM [$^{15}$N]-HCA in 50 mM sodium phosphate pH 7.4 with 1.3 molar equivalents of compound 2 (green) or compound 2 (blue).
**Figure S6**  Intermolecular contacts in phosphate for HCA-2 identified by NMR spectroscopy. A) Selected region of the superposition of $^1$H, $^{15}$N-HSQC spectra of HCA-2 (green) and HCA-3 (blue) in phosphate buffer (from Figure S6B). B) $\Delta\delta_{H,N}$ of HCA-2 compared to HCA-3, calculated as in Figure 2B. C) Each observed amide is represented as a sphere on the structure of HCA (chain A from PDB ID 4LP6) and colored as in (B).
**Figure S7** Analysis of compound 2 by HPLC and ESI-MS. A) RP-HPLC (Jasco PU-2089 pump) Macherey–Nagel Nucleodur C18 gravity column (4.6×100 mm, 5μm). The mobile phase was composed of 0.1 % (v/v) TFA/H₂O (solvent A) and 0.1 % TFA/CH₃CN (solvent B) with a 5-100% solvent B gradient over 15 min (tᵣ =8.2 min). Monitoring was performed by UV detection at 300 nm with a diode array detector (Jasco UV-2077). B) HRMS (Thermo Exactive Orbitrap) in negative mode: m/z calculated for [C₈₀H₇₁N₁₄O₂₀S]⁻: 1579.4695; found: 1579.4753.
Figure S8  Analysis of compound 2 by $^1$H NMR. A) 1D $^1$H NMR of compound 2 in DMSO-d$_6$ at 300 MHz and 298 K. B) 1D $^1$H NMR of compound 2 in DMSO-d$_6$ with 1% trifluoroacetic acid at 300 MHz and 298 K.