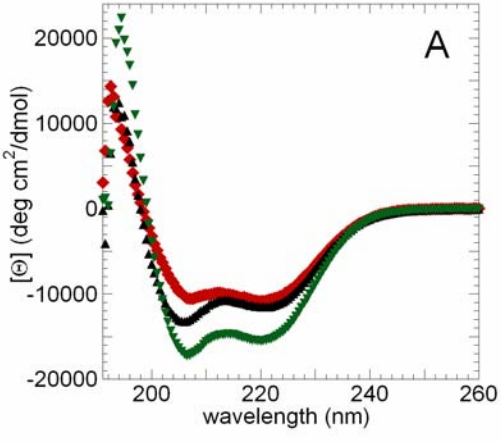
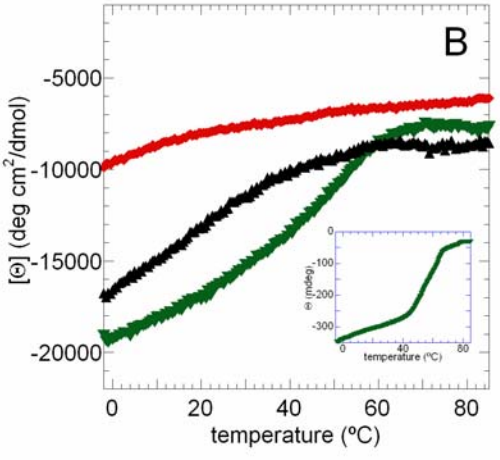
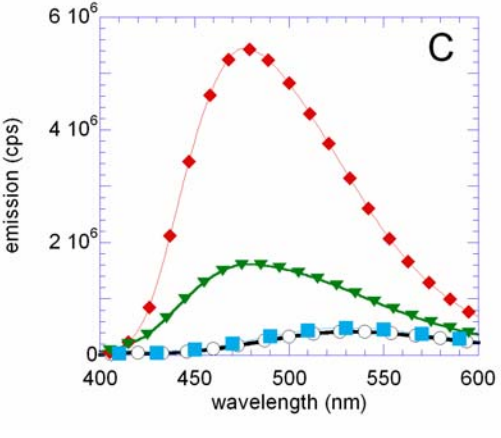
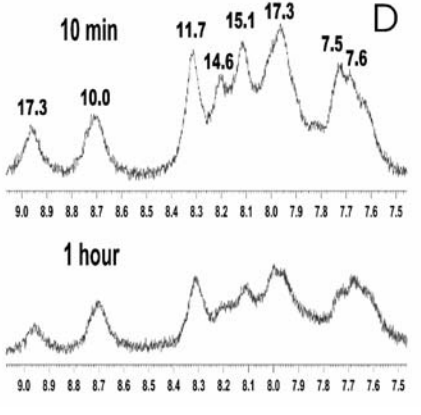

A
20000
10000
0
-10000
-20000
[Θ] (deg cm2/dmol)
200
220
240
260
wavelength (nm)


B
-5000
-10000
-15000
-20000
[Θ] (deg cm2/dmol)
0
20
40
60
80
temperature (ºC)
0
-100
-200
-300
Θ (mdeg)
0
40
80
temperature (ºC)


C
6 10^6
4 10^6
2 10^6
0
emission (cps)
400
450
500
550
600
wavelength (nm)


D
10 min
17.3
10.0
11.7
14.6
15.1
17.3
7.5
7.6
9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5
1 hour
9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5

FOR SUPPORTING INFORMATION

Supporting Figure 6 legend

A. Far UV-CD spectra of KIA5 ♦, KIA7Δ ▲, and KIA7I ▼ in 0.5 M sodium sulfate, 10 mM Na/HAc, pH 5 at 25ºC. The concentration of the KIA species is 120 μM. The same procedures were used as described in the Methodology paragraph of Supporting Figure 1, except for the salt content and concentration.

B. Thermal denaturation of KIA5 ♦, KIA7Δ ▲, and KIA7I ▼ in 0.5 M sodium sulfate, 10 mM Na/HAc, pH 5. The concentration of the KIA species is 120 μM. Inset: Thermal unfolding of a more concentrated (≈ 1mM) KIA7I sample in 1.1 M sodium sulfate, 10 mM Na/HAc, pH 5. Note that under these highly stabilizing conditions, the KIA7I thermal transition becomes more cooperative and shifts towards higher temperatures. For KIA5, KIA7Δ and some KIA7I trials, refolding upon recooling was incomplete. Please see the Methodology paragraph of **Supporting Figure 1** for a description of the procedures used to carry out these thermal unfolding experiments.

C. The fluorescence spectra of ANS alone ○, or in the presence of KIA7 ■ , KIA7I ▼, or KIA5 ♦ are shown. KIA7 induces partically no enhancement in the fluorescence of ANS, as was previously observed (3). This is a characteristic of a well-folded protein. KIA7I induces a moderate (≈3 fold) enhancement in ANS fluorescence. Proteins in the molten globule state (Semisotnov *et al.,* Biopolymers **31**, 119-128 (1991)) and some poorly packed molecules of the KIA series (3) induce significantly higher ASN fluorescence. One explanation for the moderate but not high enhancement of ANS

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Supporting Figure 6 legend, cont.

fluorescence by KIA7I is that the hydrophobic surface covered by Tyr or Phe side chains in KIA7 or KIA7F has become exposed or less well packed in KIA7I, whereas the tight packing in the center of the hydrophobic core is maintained.

Methodology: The Enhancement of ANS Fluorescence. Fluorescence spectra of 120μM 1-anilino-naphthalene-8-sulfonate (ANS), in the presence and abscence of KIA molecules (120μM) were recorded (½ sec per nm, 1 nm increments) at 2.0ºC on a Fluormax-4 instrument equipped with a Peltier temperature control unit. The excitation wavelength was 365 nm and emission spectra were recorded between 400 and 600 nm. Dry nitrogen gas was blown into the sample chamber to prevent water vapor condensation. Samples were incubated overnight on ice and ≥4 minutes in the sample compartment prior to measurement in a 3 x 3 mm Hellma QS cuvette (volume= 100 μL). A reference solution containing buffer only (0.5 M sodium sulfate, 10 mM TRIS, pH 7.3) showed an essentially flat baseline equivalent to double-distilled, deionized water.

D. H/D exchange of KIA7I in 0.5 M sodium sulfate. The amide proton region of the 1D ^{1}H-NMR spectra ten minutes (top panel) and one hour (bottom panel) after the dissolving protonated KIA7I in D_2O containing 0.5 M Na_2SO_4 and 10 mM Na/HAc(d_3) at pH* 4.9, 5 ºC. The values of the protection factors are shown over each peak. For these unassigned spectra, the protection factors were calculated assuming the order of observed exchange.

FOR SUPPORTING INFORMATION

Supporting Figure 6 legend, cont.

rates (slow to fast) matches the order (slow to fast) of the intrinsic exchange rates calculated using the sequence and the parameters of Bai *et al.,* (53).