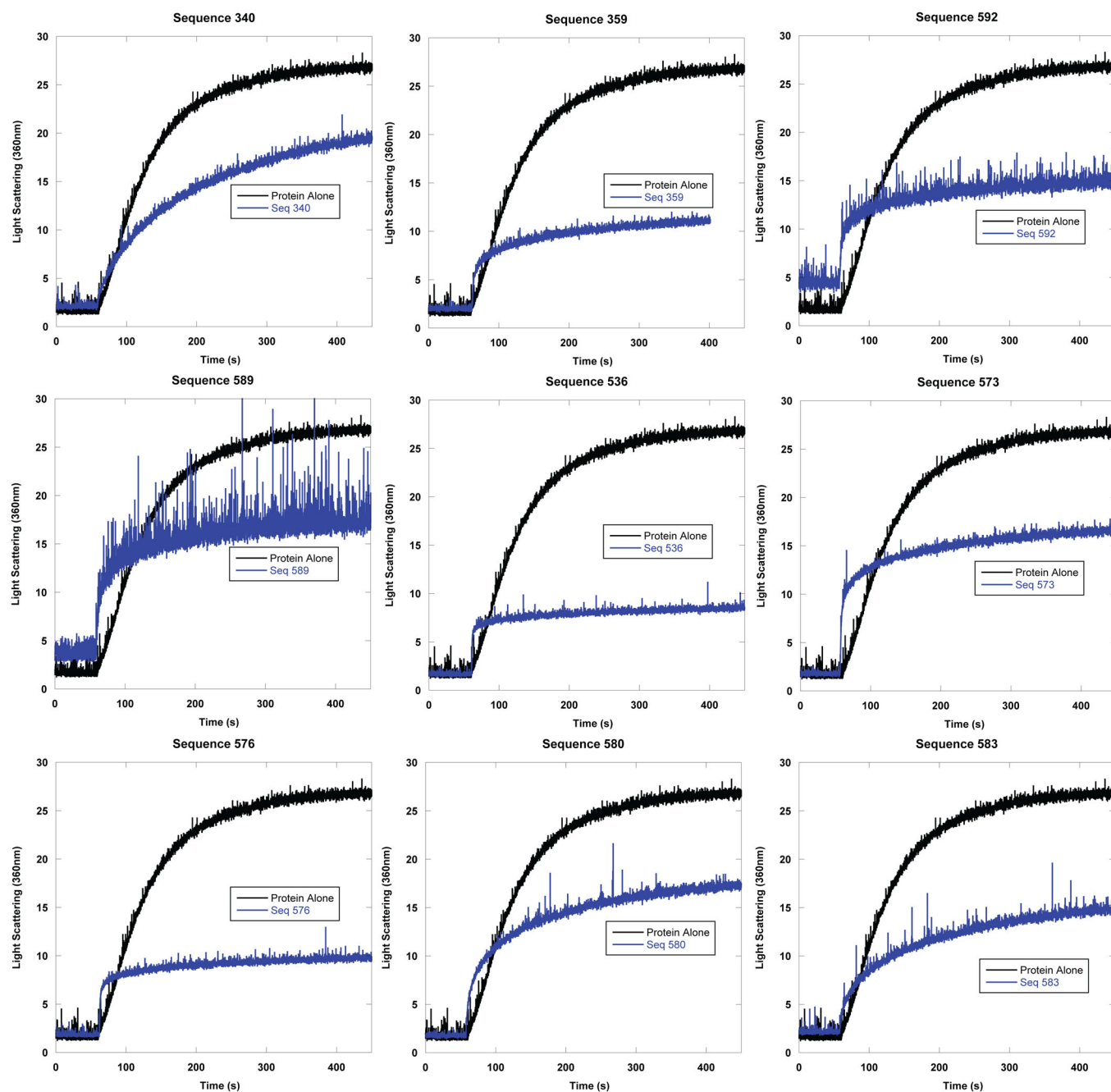
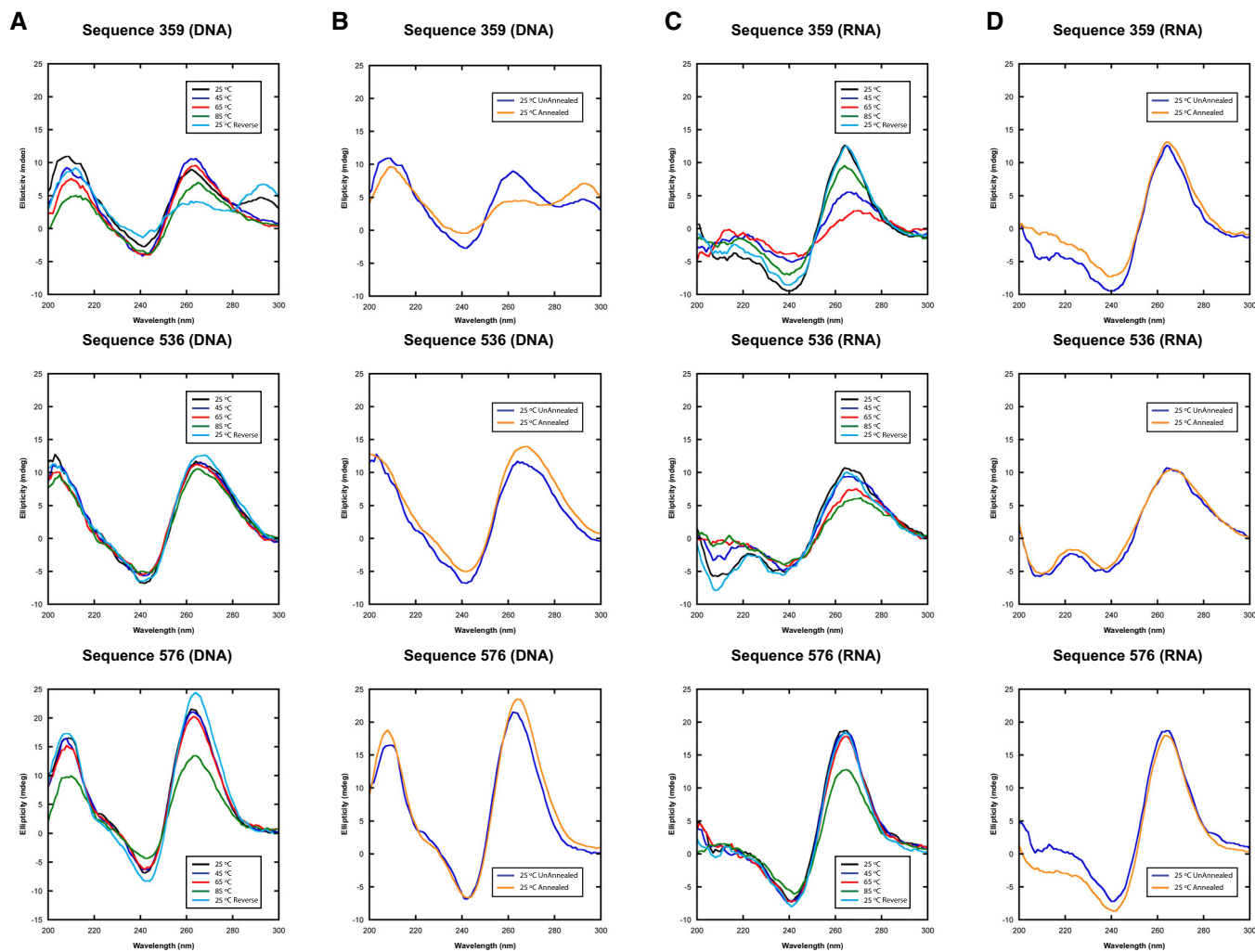


## Expanded View Figures



**Figure EV1.** Representative examples of chemical aggregation tests of multiple quadruplex-containing sequences with citrate synthase.

Representative examples of right angle light scattering of chemically denatured citrate synthase with quadruplex-containing sequences measured via fluorimeter. DNA strand to protein ratio is 2:1.

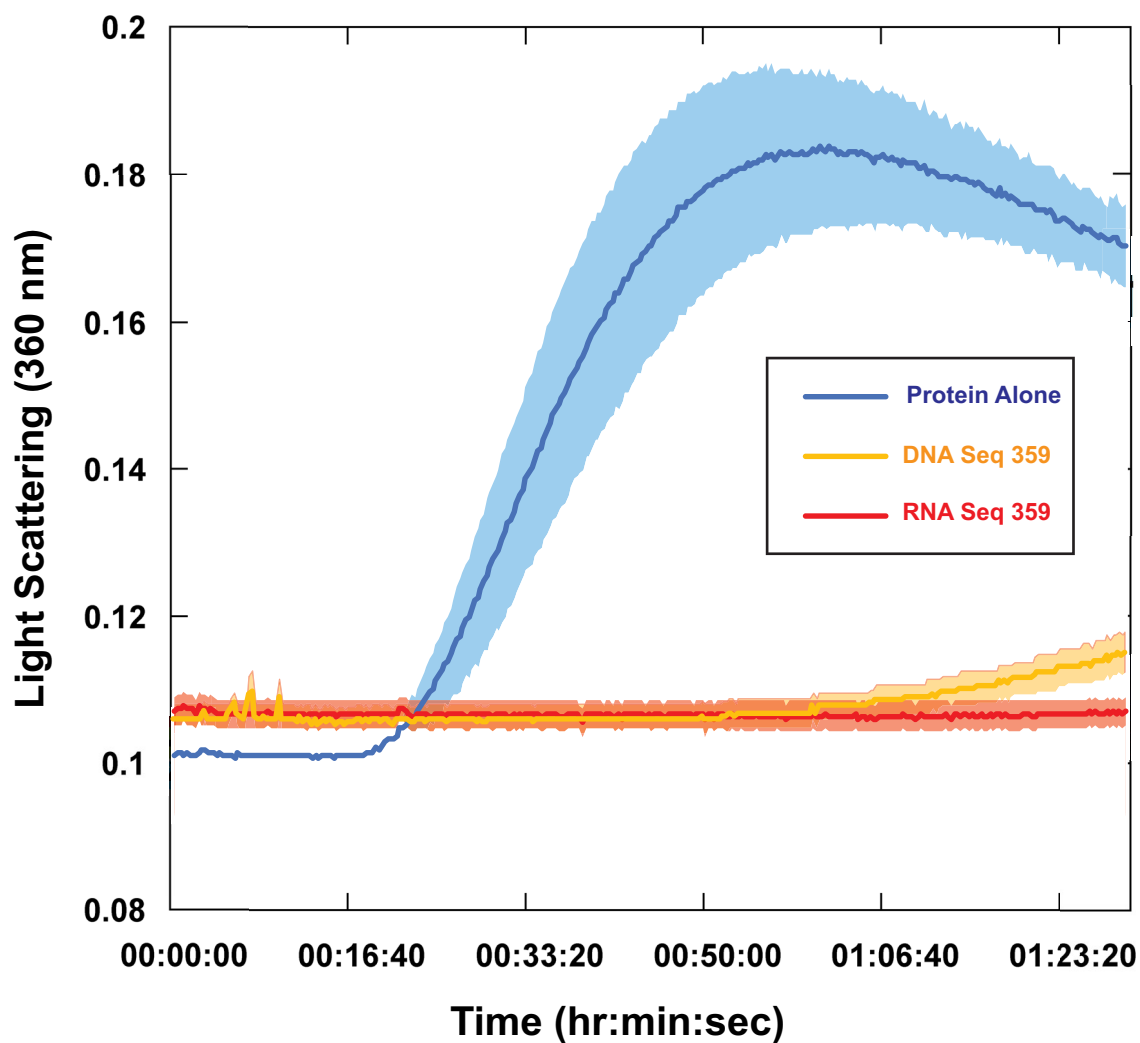


**Figure EV2. CD spectra of select 20mers (DNA (A) and (B), and RNA (C) and (D)) in 10 mM pH 7.5 potassium phosphate.**

The use of potassium phosphate here was to better mimic the initial aggregation screen in which potassium was used in the HEPES buffer.

A, C The thermal stability of quadruplex-containing sequences as measured by CD spectroscopy where each line represents a wavelength scan at the indicated temperature.

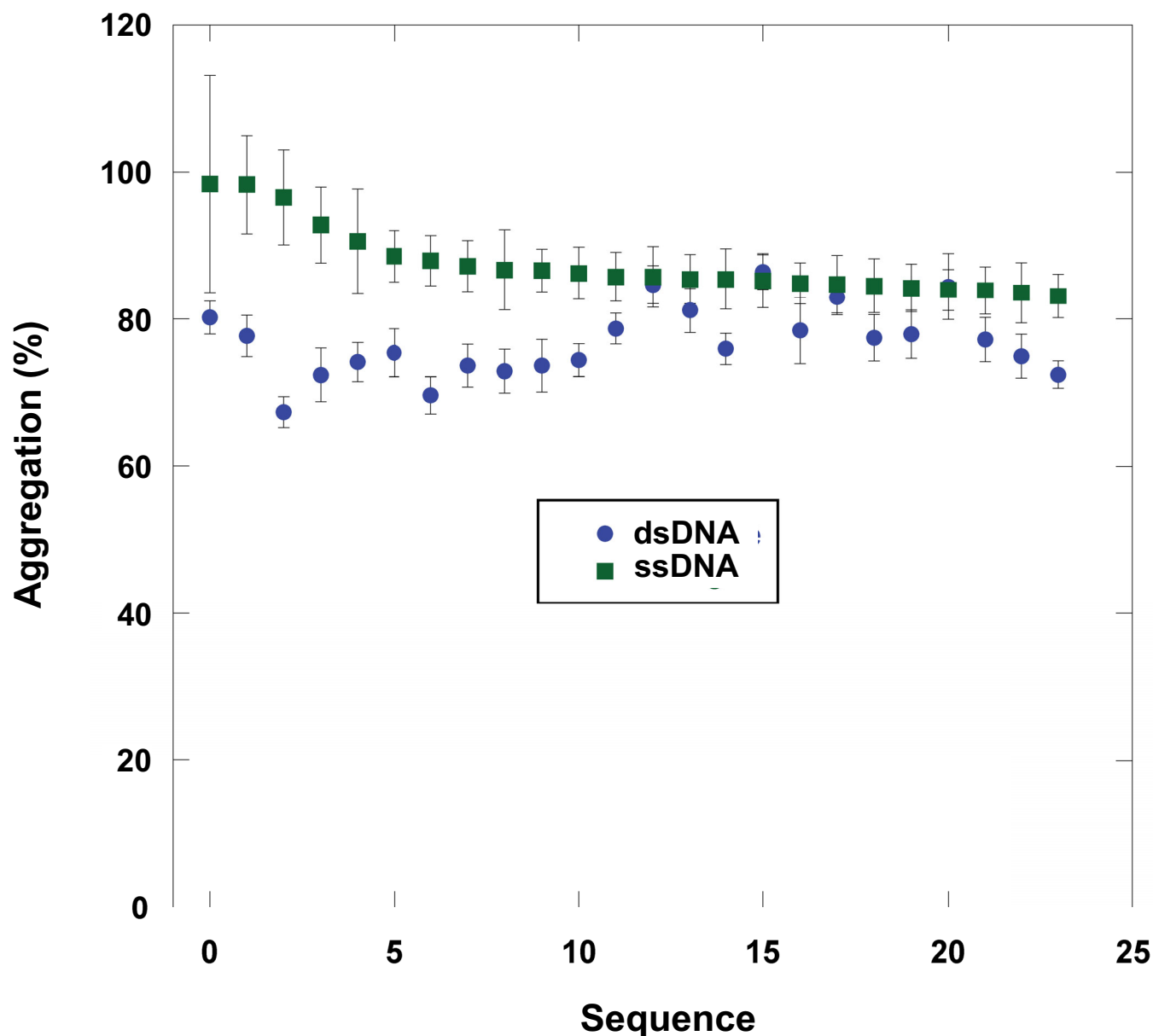
B, D The secondary structure of the same quadruplex-containing sequences at 25°C prior to annealing or after annealing at 25°C.



**Figure EV3.** Comparison of holdase activity of RNA and DNA counterparts of Sequence 359 using citrate synthase heat denaturation.

Data presented as means  $\pm$  SE ( $n = 3$ ) of technical triplicates.

Source data are available online for this figure.



**Figure EV4. Holdase activity of ssDNA toward citrate synthase compared to its duplexed counterpart as measured by heat denaturation.**

Data presented as mean  $\pm$  SE ( $n = 3$ ) of technical triplicate.

Source data are available online for this figure.

**Figure EV5. The effect of nucleic acids on the fluorescence of wtGFP.**

A Expression vector constructs. Both vectors are under the control of pBAD promoter, which is induced by 0.2% *L*-Arabinose.

B Cellular fluorescence assay of wtGFP in the presence or absence of protein folding enhancing factors. White bars (+Empty IN and +Seq42) represent negative controls. The data are presented as mean  $\pm$  SD ( $n = 3$ ) of technical triplicate.

C *In vitro* refolding of wtGFP in the presence or absence of htDNA. GFP refolding curve assessing the fluorescence of GFP over a 60-minute incubation period, with denatured GFP both in the presence of htDNA ( $n = 6$ ) and absence of htDNA ( $n = 6$ ). Non-denatured GFP (Native) with htDNA ( $n = 4$ ) was used as a control. Data are displayed as the mean of each experimental condition normalized to the blank with error bars represented as the Standard Error. All samples tested with technical replicates.

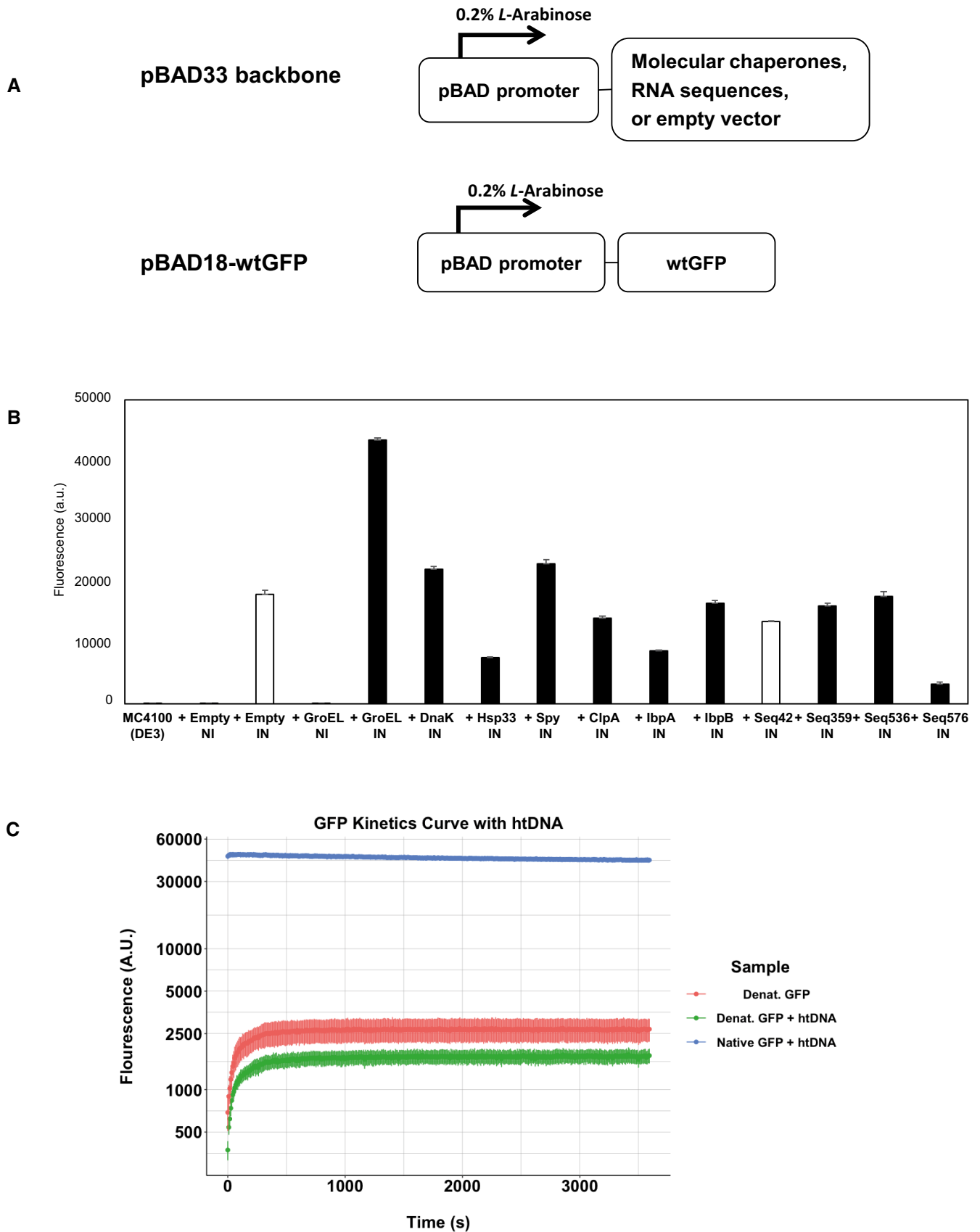


Figure EV5.