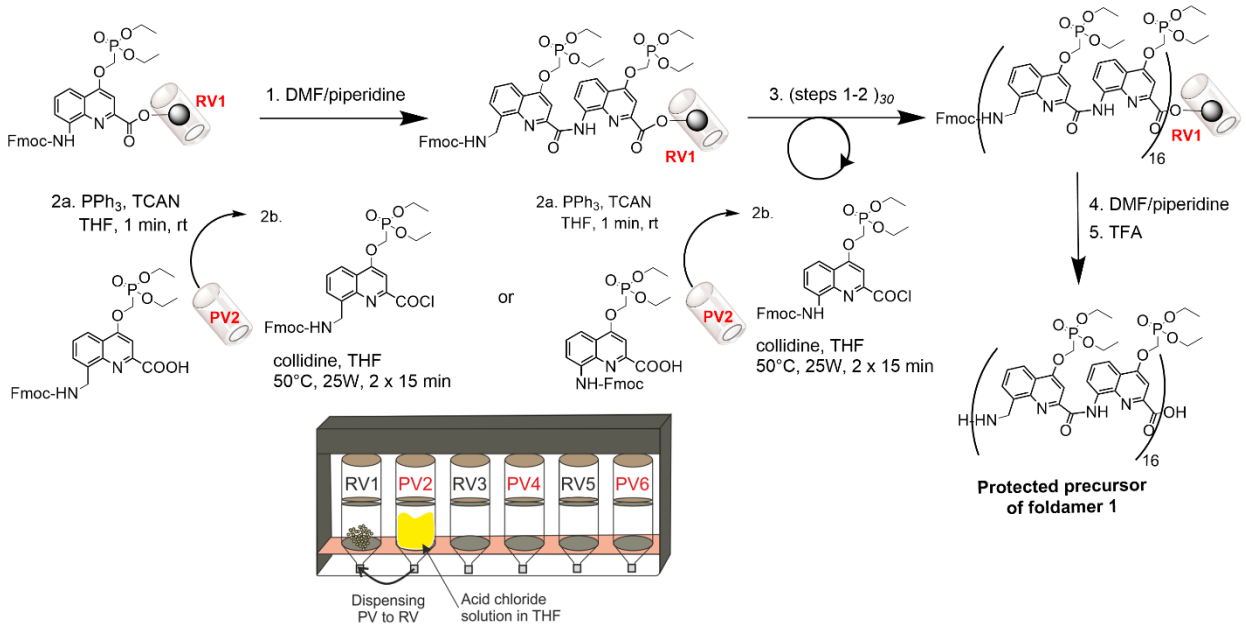
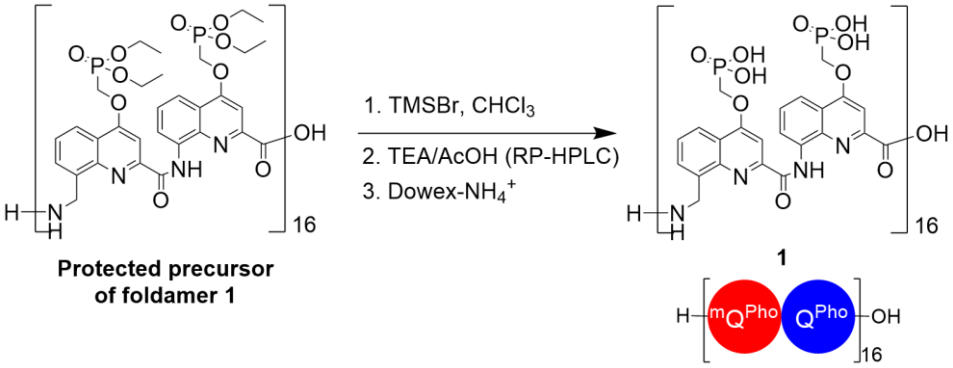
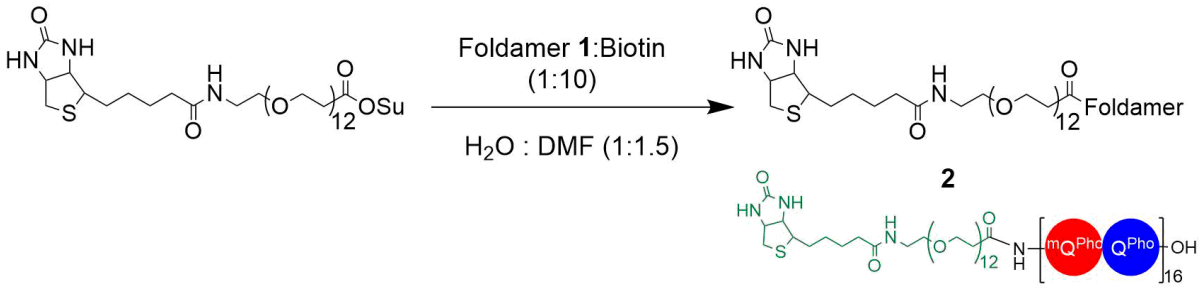
1. Supplementary Schemes and Figures



Scheme S1. Solid phase foldamer synthesis (SPFS) protocol developed for the automation of the aromatic oligoamides and exemplified for the protected precursor of foldamer **1** (32 mer). At the bottom a schematic representation of the Chorus synthesizer with reaction vessels (RVs) and preactivation vessels (PVs) used during the coupling cycles.



Scheme S2. Removal of the diethyl ester protection of the phosphonate side chains followed by reversed-phase (RP) high performance liquid chromatography (HPLC) and ion exchange (Dowex) to deliver foldamer **1** with the side chains as water-soluble ammonium phosphonate salts.



Scheme S3. Synthesis of biotinylated foldamer **2**.

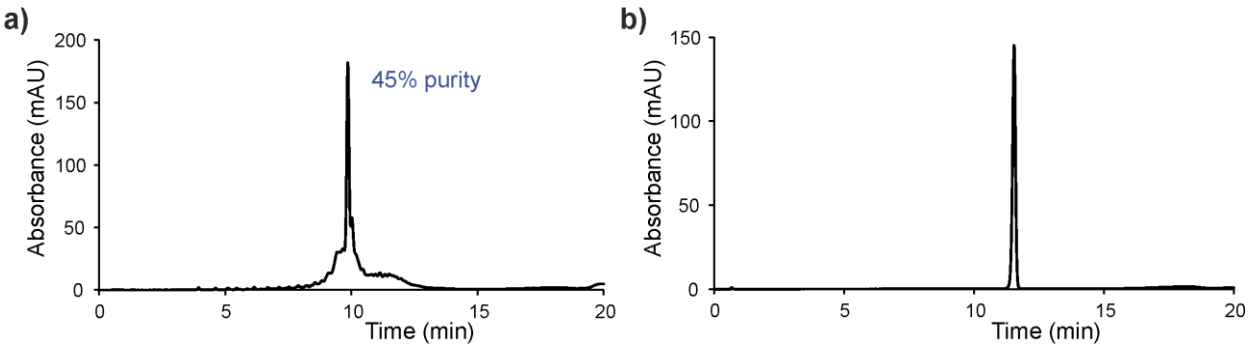


Figure S1. RP-HPLC chromatograms of the **protected precursor of foldamer 1** (bearing diethyl phosphonate side chains) after cleavage from the resin (a) and after purification (b). Elution conditions: Nucleodur C8 Gravity column, 30–70% B over 15 min where A was water + 0.1% TFA and B was acetonitrile + 0.1% TFA; 50 °C; UV detection at λ = 300 nm.

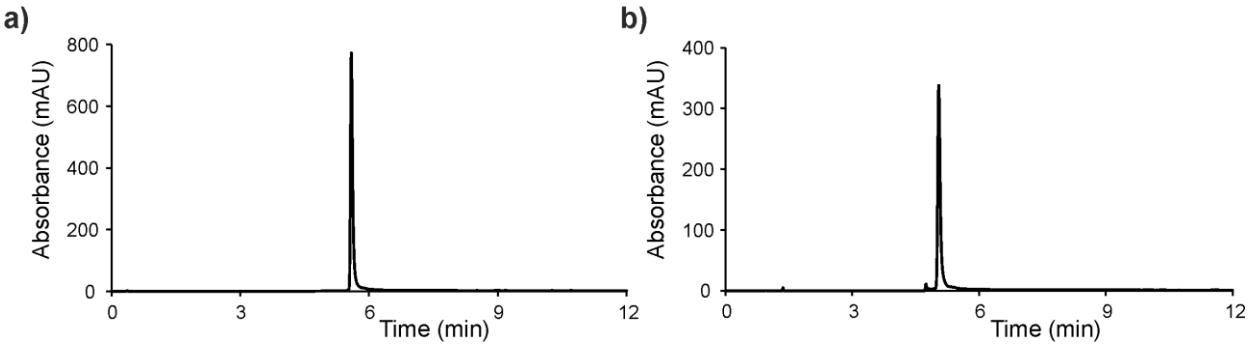


Figure S2. RP-HPLC chromatograms of foldamers **1** (a) and **2** (b). Elution conditions: Nucleodur C18 HTec column, 0–100% B over 10 min where A was 12.5 mM triethylammonium acetate (TEAA) in water pH 8.5 and B was 12.5 mM TEAA in water:acetonitrile 3:1 vol/vol pH 8.5; 25 °C; UV detection at λ = 300 nm.

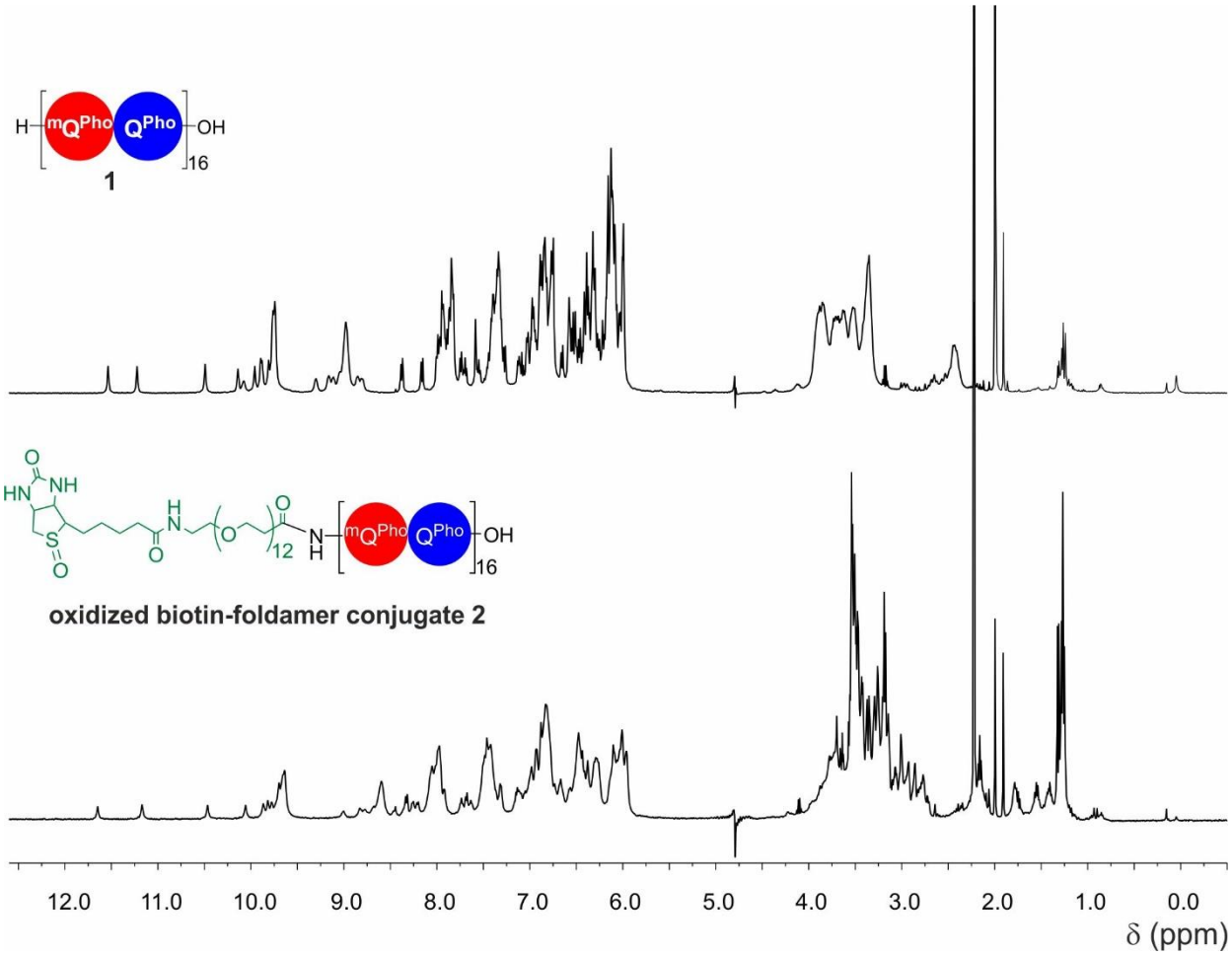


Figure S3. ^{1}H NMR spectra (500 MHz) in H_2O/D_2O 9:1 (vol/vol), 50 mM NH_4HCO_3 at 298 K of foldamer **1** and the oxidized form of biotin-foldamer conjugate **2**.

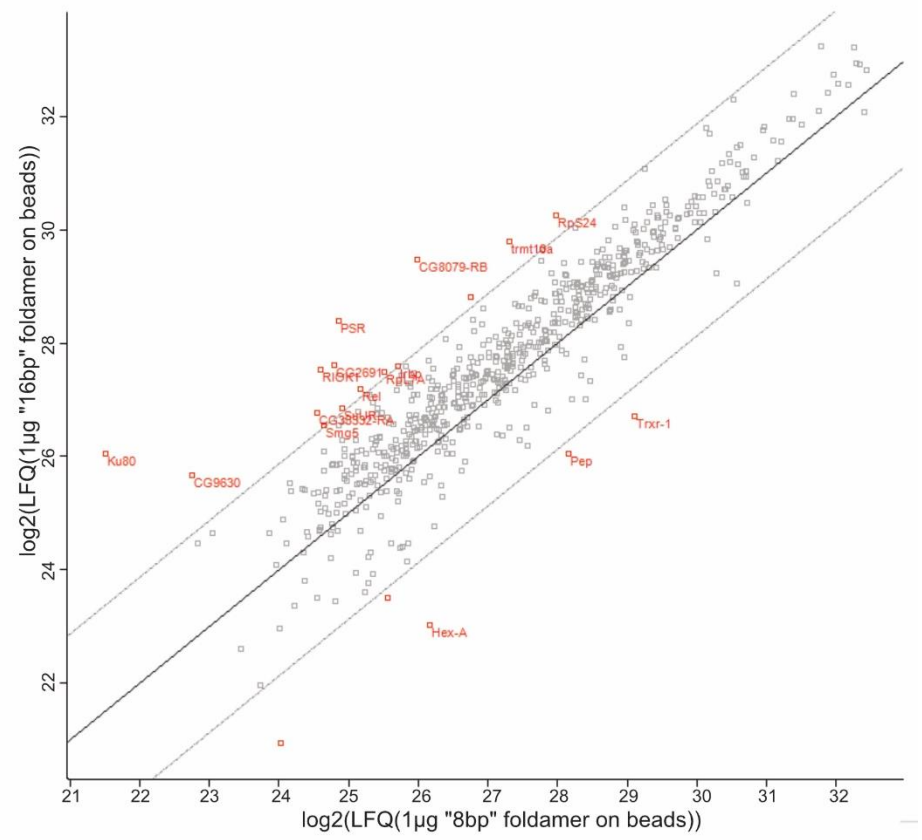


Figure S4. Scatterplot for mean intensities of proteins in Pulldown from DREX with 1µg biotinylated foldamer of “8base pair” or “16 base pair” (“16bp” in all other experiments of this study) length. Solid line= x, Dash-dotted lines= x+sd and x-sd. N=3

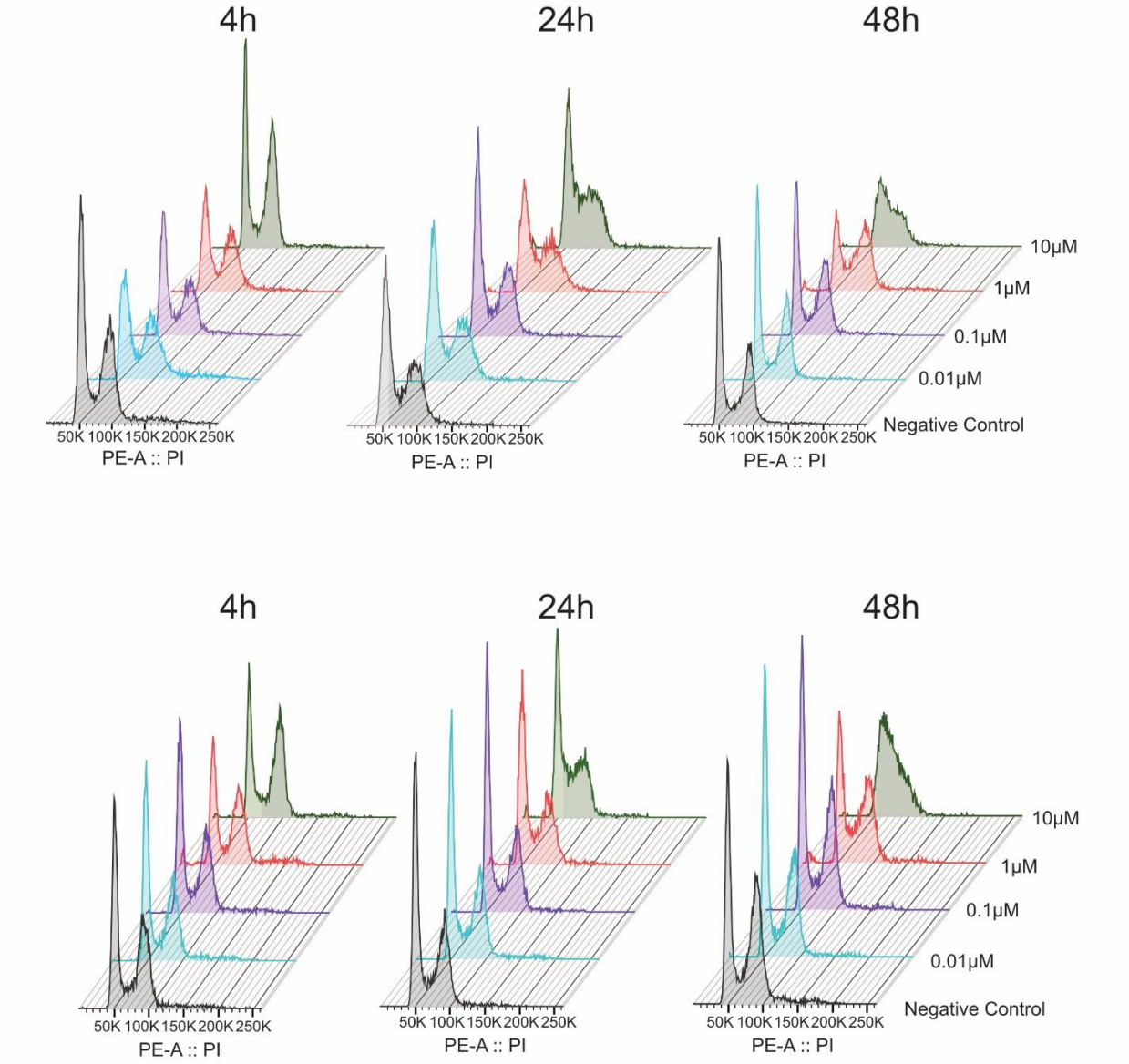


Figure S5. Cell cycle profiles of replicates 2 and 3 after 4h, 24h, and 48h of treatment with different concentrations of foldamer in serum, determined by flow cytometry with PI stain.

2. Supplementary Tables

Table S1. Interference Protein list for interference experiment with foldamer **1** including log2(LFQ) mean values for different conditions, assignment to clusters, Majority protein Ids, Protein names, and Gene names.

Table S2. Pulldown Protein list of all proteins found via LC-MS in pulldown experiment with biotinylated foldamer **2,** including log2(LFQ) mean values for beads only control and foldamer on beads, significance (FDR=0.05) as foldamer binder (where indicated as +), -LOG(P-value), Difference, Majority protein Ids, Protein names, and Gene names.

Table S3. Cell Cycle Stages Proportions of cells in each cell cycle stages for all concentrations, all time points, and replicates.