Supporting Information

Synthetic α- L-Threose Nucleic Acids Targeting BcL-2 Show Gene Silencing and In Vivo Antitumor Activity for Cancer Therapy

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Scheme S1. Synthetic scheme and structures of TNA polymer and its intermediates.

Figure S1. MALDI-TOF spectrum for anti-Bcl-2 TNA of m/z calcd 5608.2327; found 5608.5571 [M⁺].
Figure S2. MALDI-TOF spectrum for scramble TNA of m/z calcd 5502.2053; found 5502.8813 [M⁺].

Figure S3. MALDI-TOF spectrum for TNA-Cy3 of m/z calcd 5505.3800; found 5494.9883 [M⁺].
Figure S4. Native PAGE analysis of the binding specificity of the anti-Bcl-2 TNA with its complementary (a) sense-Bcl-2 DNA and (b) sense-Bcl-2 RNA. Lane 1: anti-Bcl2 TNA; Lane 2: sense-Bcl-2 DNA/RNA; lane 3: a mixture of anti-Bcl-2 TNA and sense-Bcl-2 DNA/RNA. A unique band (lane 3) with altered mobility compared with TNA (lane 1) and DNA or RNA (lane 2) was observed. Electrophoresis was performed with a current of 30 mA at 4 °C for 6 h.

Figure S5. CLSM images of MCF-7 cells incubated with TNA-Cy3 for 12 h. Nucleus was stained with Hoechst 33258 dye. Scale bar = 10 µm.
Figure S6. CLSM images showing a large number (~500) of MCF-7 cells incubated with TNA-Cy3 for 12 h. Nucleus was stained with Hoechst 33258 dye. Scale bar = 250 µm.
Figure S7. 3D reconstruction from 120 confocal images of MCF-7 cells incubated with TNA-Cy3 (green) for 12 h. Nucleus was stained with Hoechst 33258 dye (blue).
**Figure S8.** Flow Cytometry analysis of the endocytic mechanism of TNA cellular uptake. MCF-7 cells without any treatment was employed to determine the background Cy3 fluorescence intensity. MCF-7 cells treated with TNA-Cy3 incubation was set as control. An increase of fluorescence signal in each sample was analyzed after the deduction of the background signals obtained and converted the results to the % of cellular uptake.