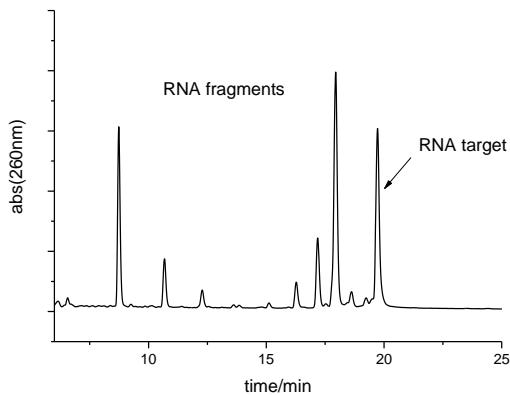


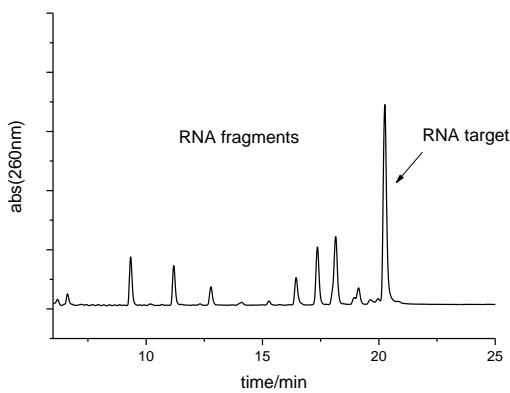
## Supplementary

**Figure S1.** IE-HPLC analysis of 4-nucleotide bulge RNA cleavage reactions in the presence of PNAzyme1 and RNA (1:1, PNAzyme:RNA). Reactions were carried out using 100  $\mu$ M effective concentration of  $Zn^{2+}$  and were analyzed at the 24 h time point (pH 7.4, 37 °C).

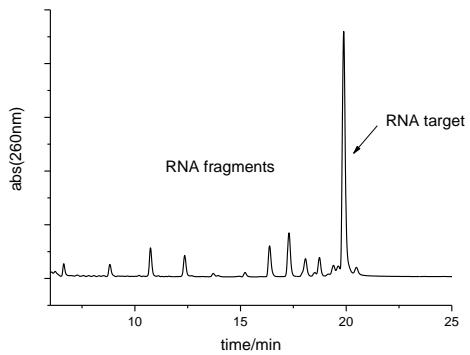
**RNA1,** (4-nucleotide bulge: 5'-AAAA-3')



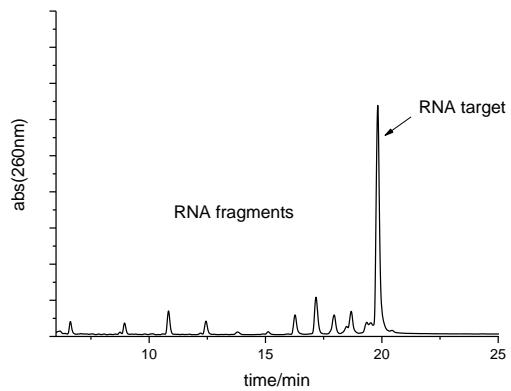
**RNA2,** (4-nucleotide bulge: 5'-AAAG-3')



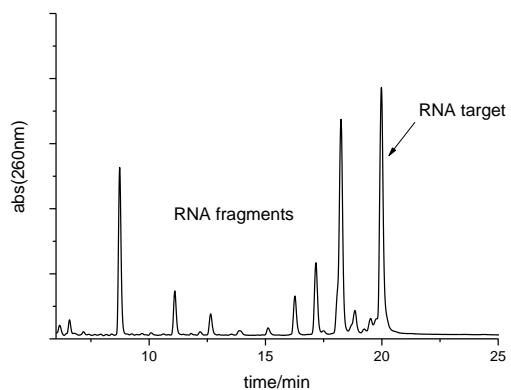
**RNA3**, (4-nucleotide bulge: 5'-AAAC-3')



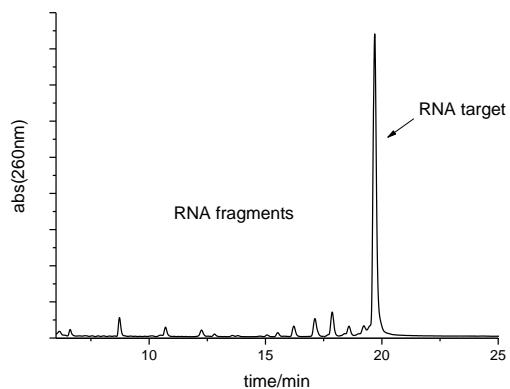
**RNA4**, (4-nucleotide bulge: 5'-AAAU-3')



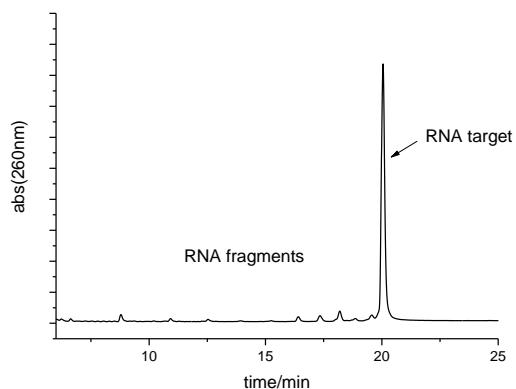
**RNA5**, (4-nucleotide bulge: 5'-AAGA-3')



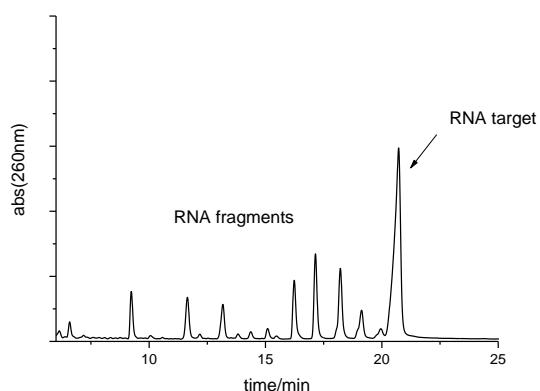
**RNA6, (4-nucleotide bulge: 5'-AACCA-3')**



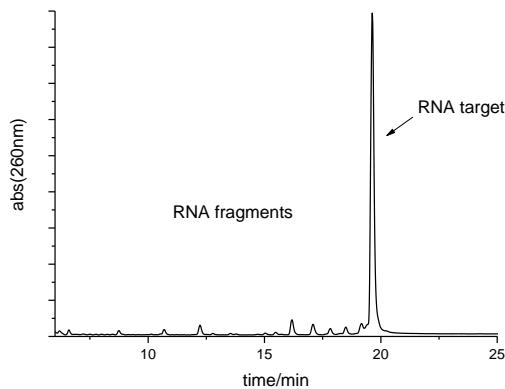
**RNA7, (4-nucleotide bulge: 5'-AAUA-3')**



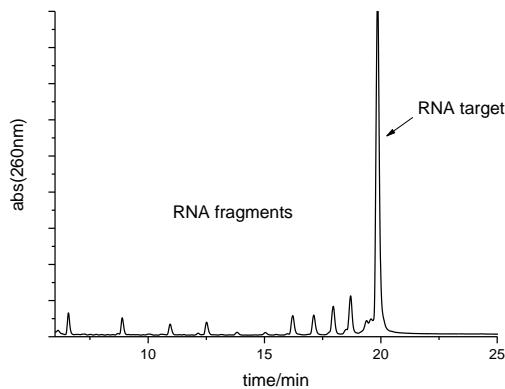
**RNA8, (4-nucleotide bulge: 5'-AAGG-3')**



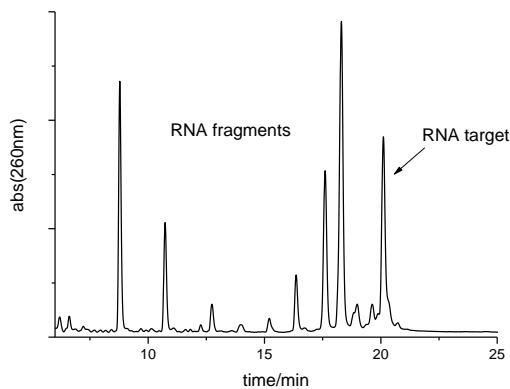
**RNA9, (4-nucleotide bulge: 5'-AAC<sub>4</sub>-3')**



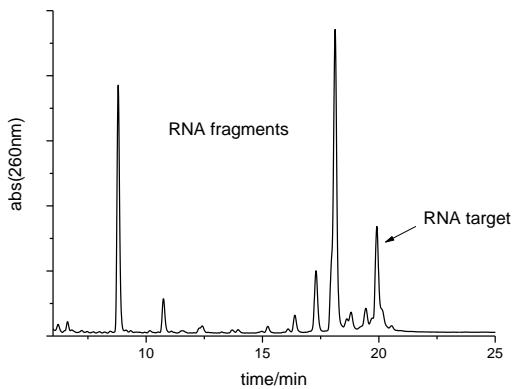
**RNA10, (4-nucleotide bulge: 5'-AAU<sub>4</sub>-3')**



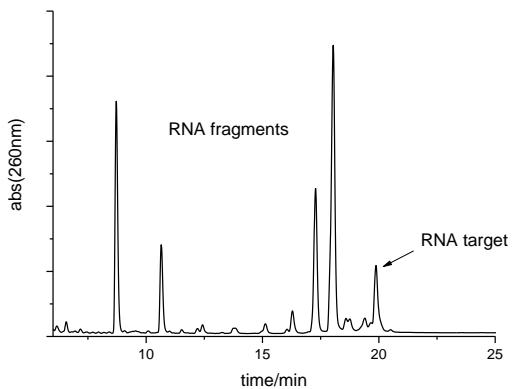
**RNA11, (4-nucleotide bulge: 5'-AGA<sub>4</sub>-3')**



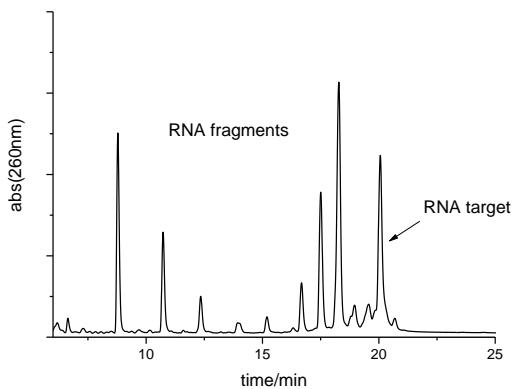
**RNA12, (4-nucleotide bulge: 5'-ACAA-3')**



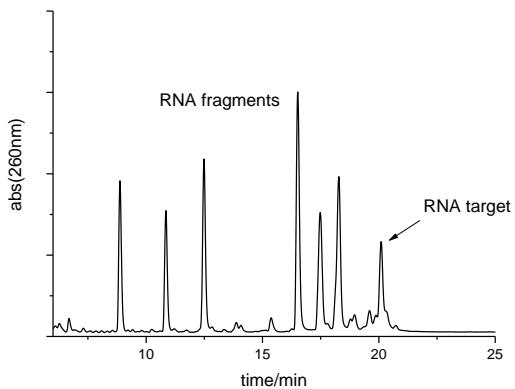
**RNA13, (4-nucleotide bulge: 5'-AUAA-3')**



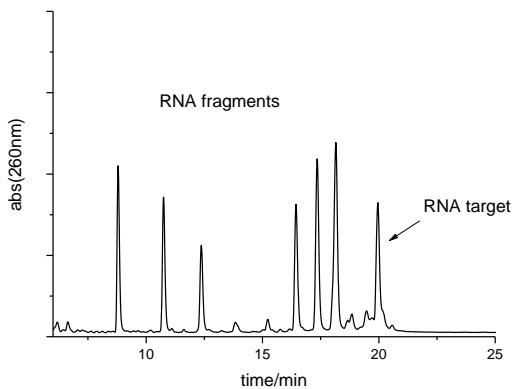
**RNA14, (4-nucleotide bulge: 5'-GAAA-3')**



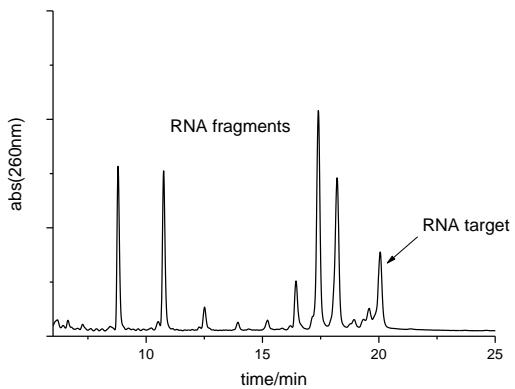
**RNA15**, (4-nucleotide bulge: 5'-CAAA-3')



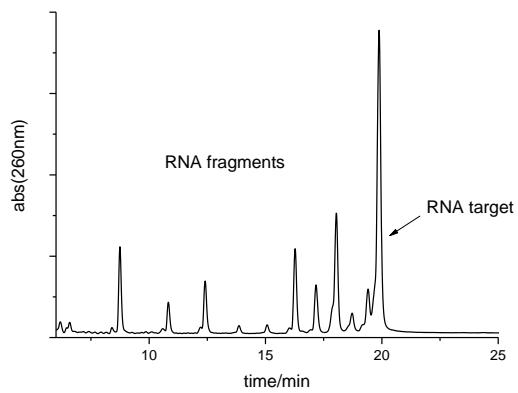
**RNA16**, (4-nucleotide bulge: 5'-UAAA-3')



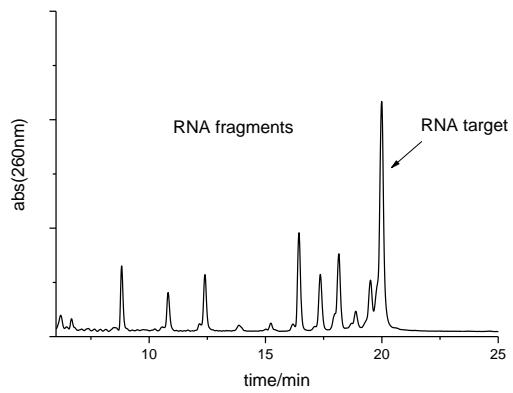
**RNA17**, (4-nucleotide bulge: 5'-UUAA-3')



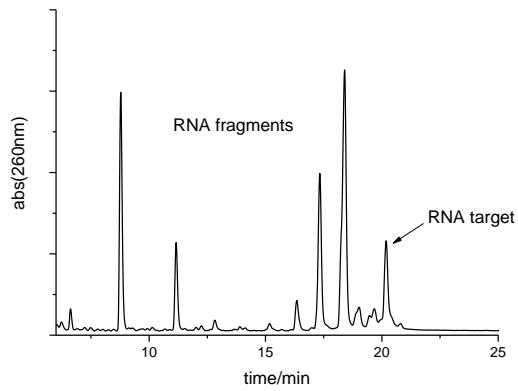
**RNA18, (4-nucleotide bulge: 5'-UUUA-3')**



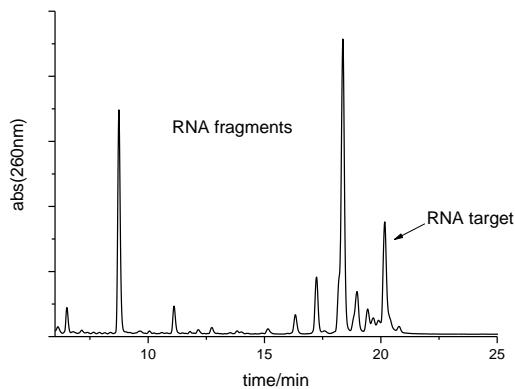
**RNA19, (4-nucleotide bulge: 5'-UAUA-3')**



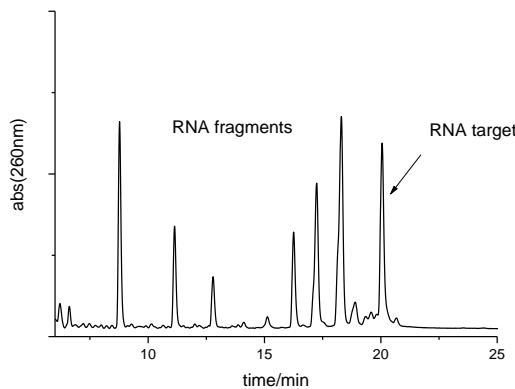
**RNA20, (4-nucleotide bulge: 5'-AUGA-3')**



**RNA21**, (4-nucleotide bulge: 5'-ACGA-3')

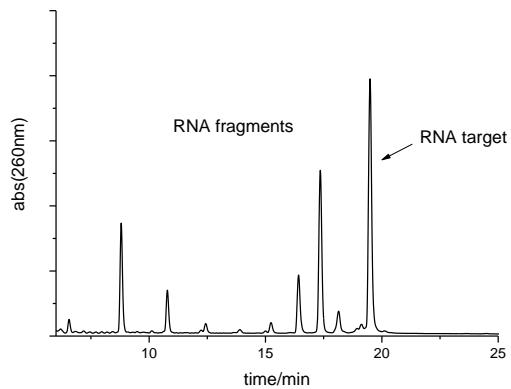


**RNA22**, (4-nucleotide bulge: 5'-CUGA-3')

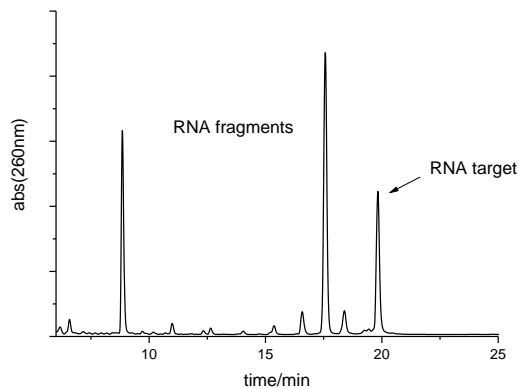


**Figure S2.** IE-HPLC analysis of 3-nucleotide bulge RNA cleavage reactions in the presence of **PNAzyme1** and RNA (1:1, PNAzyme:RNA). Reactions were carried out using 100  $\mu$ M effective concentration of  $Zn^{2+}$  and were analyzed at the 24 h time point (pH 7.4, 37 °C).

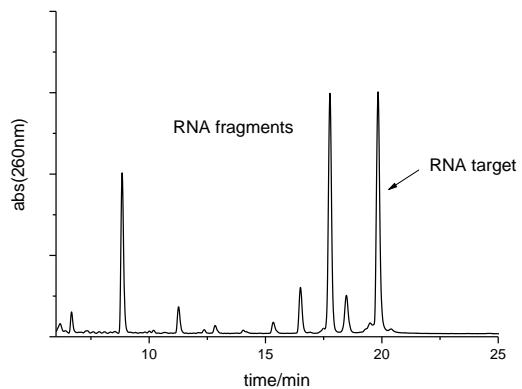
**RNA23**, (3-nucleotide bulge:  $5'$ -AAA- $3'$ )



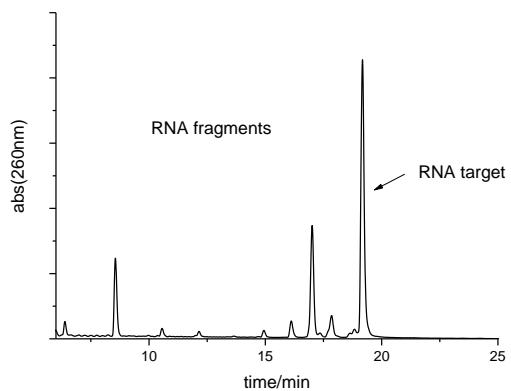
**RNA24**, (3-nucleotide bulge:  $5'$ -AUA- $3'$ )



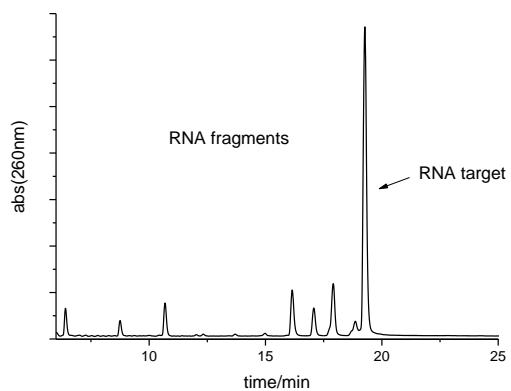
**RNA25**, (3-nucleotide bulge:  $5'$ -AGA- $3'$ )



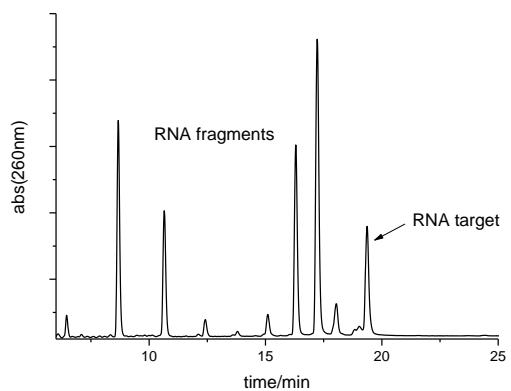
**RNA26, (3-nucleotide bulge: 5'-ACA-3')**



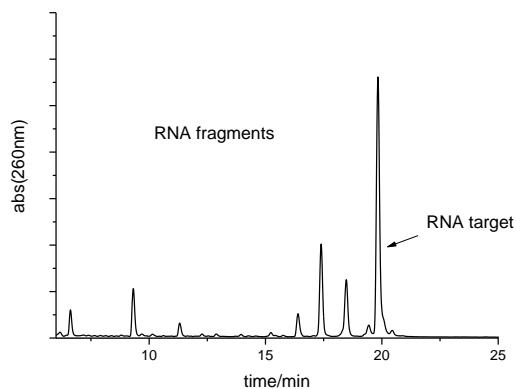
**RNA27, (3-nucleotide bulge: 5'-AAU-3')**



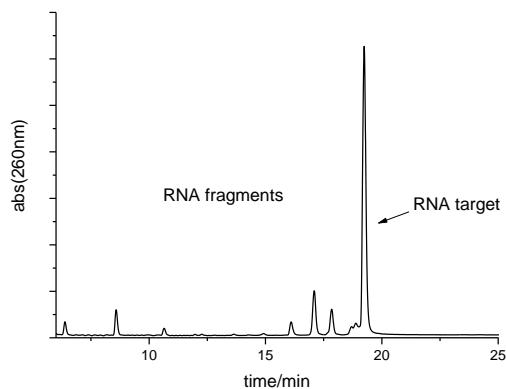
**RNA28, (3-nucleotide bulge: 5'-UAA-3')**



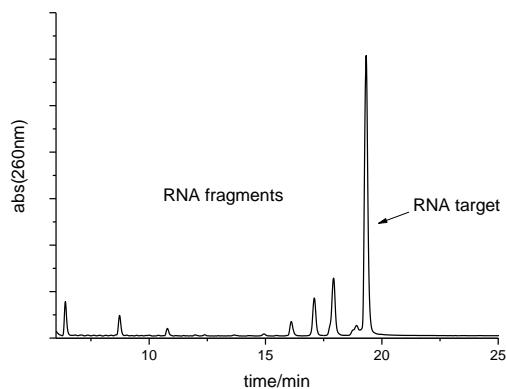
**RNA29, (3-nucleotide bulge: 5'-AUG-3')**



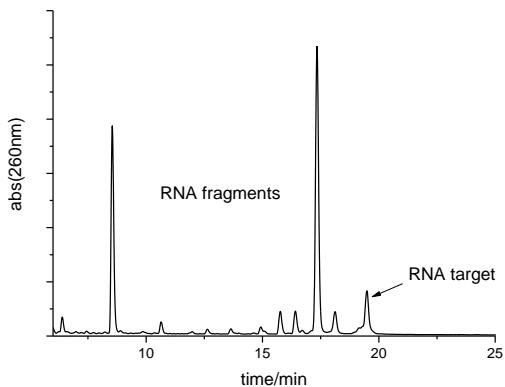
**RNA30, (3-nucleotide bulge: 5'-AUC-3')**



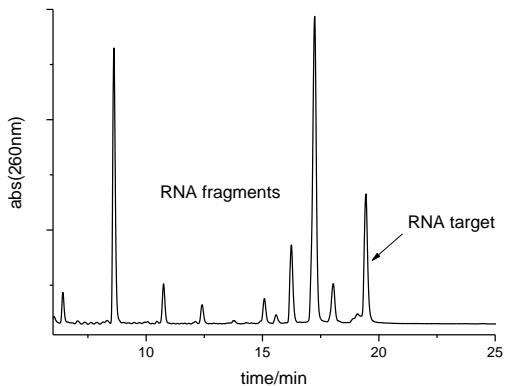
**RNA31, (3-nucleotide bulge: 5'-AUU-3')**



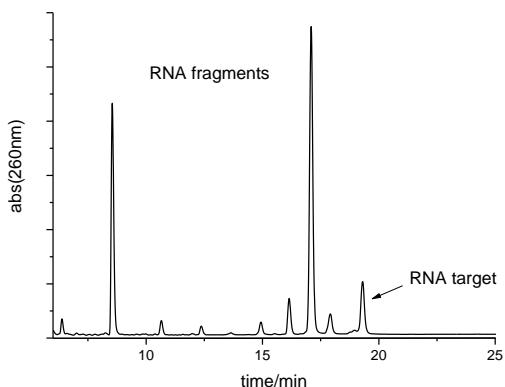
**RNA32, (3-nucleotide bulge: 5'-GUA-3')**



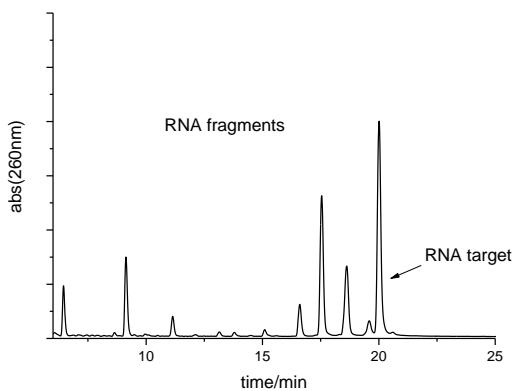
**RNA33, (3-nucleotide bulge: 5'-CUA-3')**



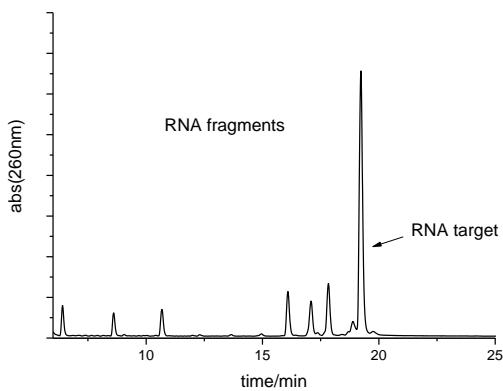
**RNA34, (3-nucleotide bulge: 5'-UUA-3')**



**RNA35, (3-nucleotide bulge: 5'-GUG-3')**



**RNA36, (3-nucleotide bulge: 5'-CUC-3')**



**RNA37, (3-nucleotide bulge: 5'-ACG-3')**

