Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (67): Effects of malignant alteration in cancer cells on the DNA G-quadruplexes and transcript mutations

(1FIBER, Konan University, 2FIRST, Konan University) ○Hisae Tateishi-Karimata1, Keiko Kawauchi2, Tatsuya Ohyama,1 and Naoki Sugimoto1,2

Keywords: Transcript mutation; Cancer cell; Malignant alteration; G-quadruplex; Potassium concentration

The DNA sequences with the potential to form G-quadruplexes locate in oncogenes or proto-oncogenes. We previously showed that the frequency of transcript mutations depends on the stability of the G-quadruplexes formed in the template DNAs.1 The G-quadruplex formation is highly responsive to surrounding conditions, particularly K+ concentration. Malignant cancer cells have a much lower K+ concentration than normal cells because of overexpression of a K+ channel; thus, G-quadruplexes may be unstable in cancer cells.

Here, we investigated physicochemically how changes of intracellular chemical environments influence G-quadruplex formation and transcription during tumor progression in cells. We designed template DNAs with a G-quadruplex (D1, D2, D3, or D4) and without G-quadruplex (Linear). Thermodynamic analysis showed that the G-quadruplexes in D2 and D4 were very stable. The effect of the G-quadruplex stability on the production of run-off transcripts was also estimated. In a normal cell (NIH3T3 cell), the transcription efficiency inversely correlated with G-quadruplex stability (Figure 1a). Interestingly, higher transcript levels were produced from templates with G-quadruplex-forming potential in the Ras-transformed cell with highly metastatic properties than in the normal cell (Figure 1b). These results suggest that in normal cell, K+ ions attenuate the transcription of certain oncogenes by stabilizing G-quadruplex structures.2 In our presentation, we will discuss how the stability of G-quadruplexes in cell is changed during tumor progression.


**Figure 1.** Effect of the G-quadruplex stability on the production of run-off transcripts (transcription efficiency in cell: TE_{in cell}). The TE_{in cell} values from each template encoded on a plasmid in (a) NIH3T3 and (b) NIH3T3 (Ha-RasV12) cells. qRT-PCR was performed to quantify run-off transcripts.