# Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (73): Effect of G-quadruplex stability change on transcriptional repression in cancer cells

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**Keywords**: transcript mutation; cancer cell; malignant alteration; G-quadruplex; potassium ion concentration

Transcription is the first step in gene expression; it is highly regulated during both initiation and elongation.[1] DNA structures are known to affect cellular processes. We have shown that G-quadruplex formations are highly responsive to surrounding conditions including cation concentration and the G-quadruplexes in the template DNA induce transcription mutation.[2] Malignant cancer cells have a much lower $K^+$ concentration than normal cells, thus, G-quadruplexes may be unstable in the cells. However, relationships between G-quadruplex formation and tumor progression are still unclear.

Here, we designed and studied template DNAs (Figure 1): a linear sequence that does not have significant higher-order structure and several G-rich sequences from proto-oncogene. Transcription reaction *in vitro*, G-rich templates induced the production of arrested and slipped transcripts in a solution containing 150 mM KCl (normal conditions), although the linear sequence produced only a full-length transcript. The production efficiency of full-length and slipped transcripts from templates that formed the stable G-quadruplex was lower than that from the linear sequence. With decreasing $K^+$ concentration, which decreases G-quadruplex stability, transcription efficiencies increased. The trend in transcription efficiency versus G-quadruplex stability in normal cells was similar to that *in vitro* experiments. Interestingly, higher transcription levels from G-rich templates were observed in Ras-transformed and highly metastatic breast cancer cells than in non-transformed and control cells. These results suggest that in normal cell, $K^+$ ions attenuate the transcription of certain oncogenes by stabilizing G-quadruplex structures.[3] In our presentation, we will discuss how the stability of G-quadruplexes in cell is changed during tumor progression.

1) H. Tateishi-Karimata, N. Sugimoto *Nucleic Acids Res,* **2021**, *49,* 7839. 2) H. Tateishi-Karimata, N. Isono, N. Sugimoto, *PLoS ONE.* **2014**, *9,* e90580. 3) H. Tateishi-Karimata, K. Kawauchi, N. Sugimoto, *J. Am. Chem. Soc.* **2018**, *140*, 642.

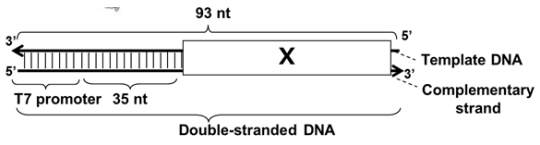


**Figure 1.** Illustration of the template DNA. The region denoted by the box marked with X contains the sequence designed to form a random coil or a G-quadruplex.