

New Data Science in Nucleic Acids Chemistry (4): Development of high-throughput screening method targeting G-quadruplexes using the pseudo-cellular system and machine learning

(¹Frontier Institute for Biomolecular Engineering Research (FIBER) Konan University, ²Graduate School of Frontiers of Innovative Research in Science and Technology (FIRST), Konan University, ³ Department of Computational Science, Graduate School of System Informatics, Kobe University)

Tatsuya Ohyama,¹ ○ Hisae Tateishi-Karimata,¹ Keiko Kawauchi,² Shuntaro Takahashi,¹ Shigenori Tanaka,³ Naoki Sugimoto,^{1,2}

Keywords: Pseudo-cellular system; G-quadruplex; Transcription; High-throughput screening; Machine learning

Nucleic-acids-targeting compounds are being screened worldwide for inhibiting diseases-related biological reactions. However, compounds optimized *in vitro* often fail to function in cells, because biomacromolecules are under molecular crowding environments in cells. Here, we developed a new pseudo-cellular system (Figure 1) for highlighting the environments inside the cell and quantitatively investigated the environmental effects on DNA G-quadruplexes, which have recently attracted attention as targets for pharmaceuticals.¹ We screened compounds that bind to the G-quadruplexes and inhibit transcription *in vitro*, in the pseudo-cellular system, and in living cells. As results, the compounds showed similar trends of transcriptional inhibition both in the living cells and the pseudo-cellular system. In the presentation, we will discuss the structural features of the ligands which bound to the G-quadruplex and inhibited transcription using machine learning analysis.

1) H. Tateishi-Karimata, K. Kawauchi, N. Sugimoto, *J. Am. Chem. Soc.* **2018**, *140*, 642.

