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Anti-tumor activity and adverse effects of a novel compound with high specificity to tetraplex DNA

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Telomerase which extends telomere sequences to the end of chromosome is overexpressed in more than 80% of cancer cells, thus it is expected as a target for developing anticancer drug. As the telomeric repeat sequences form characteristic quadruplex DNA structure, we here investigated the effects of novel compounds with improved binding specificity to quadruplex DNA structure, namely, cyclic naphthalene diimide (cNDI) and cyclic anthraquinone (cAQ), on various cultured cells.

Human cancer cell line Ca9-22, SAS, HSC-2, HeLa, and human normal keratinocytes, mouse bone marrow cells were used in this study. Cell proliferation was examined by WST-8 assay and direct counting using a hemocytometer. Gene expression was analyzed by general PCR and real-time PCR using reverse transcribed total RNA prepared from the cells.

All the derivatives of cNDI and cAQ inhibited cell growth in a dose-dependent manner, and the effect of some compounds tended to correlate with the mRNA expression level of TERT gene. Furthermore, the novel compounds showed a strong cell growth inhibitory effect against cancer-derived cell lines by comparing mouse bone marrow cells with human normal epidermal keratinocytes. The results suggested that cNDI and cAQ derivatives are considered to be promising as new anticancer agents with improved cancer specificity.