# A physicochemical study of two G-quadruplex within *KRAS* gene promoter

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In the past decades, higher-order DNA structures called G-quadruplexes (G4s) have attracted great attention as potential druggable targets since they can in principle allow a high degree of selectivity, thus minimizing adverse side effects. G4s form in relevant genomic regions and intervene in several biological processes, including the modulation of oncogenes expression, and are potential anticancer drug targets[1]. In particular, *KRAS* oncogene is involved in the pathogenesis of different types of cancers, therefore it is an important target for anticancer drug development. Its promoter region contains guanine-rich sequences able to fold into G4 structures. Here, we compared, using circular dichroism and differential scanning calorimetry as complementary physicochemical methodologies, the thermodynamic stability of the G4s formed by a shorter and a longer version of the *KRAS* promoter sequence, namely 5'-AGGGCGGTGTGGGAATAGGGAA-3' (*KRAS* 22RT), and 5'-AGGGCGGTGTGGGAAGAGGGAAGAGGGGGAGG-3' (*KRAS* 32R). Our results show that the unfolding mechanisms of *KRAS* 32R is more complex than that of *KRAS* 22RT. The different thermodynamic stability is discussed based on the recently determined NMR structures. The binding properties of TMPyP4 and BRACO-19, two well-known G4-targeting anticancer compounds, to the *KRAS* G4s were also investigated. The present physicochemical study aims to help in choosing the best G4 target for potential anticancer drugs[2].

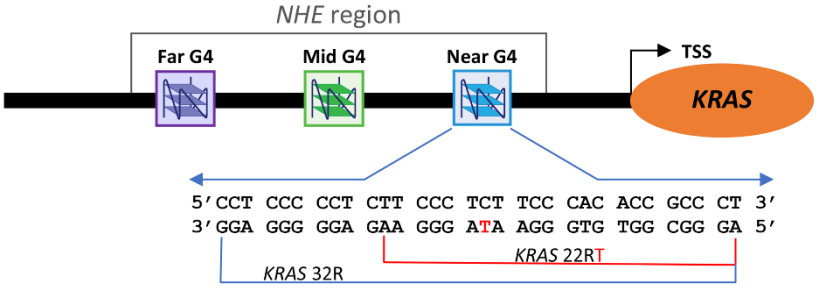


**Figure 1.** Schematic representation of the NHE region of the KRAS gene promoter.

*References*

[1] Murat, P.; Balasubramanian, S., Existence and consequences of G-quadruplex structures in DNA. *Curr. Opin. Genet. Dev.* 2014, 25, 22-29.

[2] D'Aria F., Pagano B., Petraccone L., Giancola C., *KRAS* promoter G-Quadruplexes from sequences of different length: a physicochemical study. *Int. J. Mol. Sci.* 2021, 22, 448.