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The Potential of B-myb G-quadruplex in Cancer Therapy: Insights into Formation, Small Molecule Binding and Biological Outcomes

André Miranda [1], Anne Cucchiarinni [2], Cyril Esnault Cyril Esnault [3], Jean-Christophe Andrau [3], Paula Oliveira [4], Jean-Louis Mergny [2], Carla Cruz [1]

[1] RISE-Health, Department of Chemistry, Faculty of Sciences, University of Beira Interior, Rua Marquês d'Ávila e Bolama, 6201-001 Covilhã, Portugal;, Covilhã, Portugal

[2] Laboratoire d'Optique et Biosciences, École Polytechnique, CNRS, INSERM, Institut Polytechnique de Paris, 91120 Palaiseau, France;, Paris, France

[3] Institut de Génétique Moléculaire de Montpellier, University of Montpellier, CNRS-UMR 5535, Montpellier, France, Montpellier, France

[4] Centre for Research and Technology of Agro-Environmental and Biological Sciences (CITAB), Inov4Agro, University of Trás-os-Montes and Alto Douro (UTAD, Vila Real, Portugal

The B-MYB oncogene encodes a transcription factor crucial for regulating the cell cycle and differentiation; however, abnormal expression associated with poor prognosis is observed in cancer. Gene promoter regions are enriched in guanines (G), enabling the formation of G-quadruplexes (G4), that arise from the self-folding of four G into planar arrangements stabilized by Hoogsteen bonds. G4 can play regulatory roles in gene expression due to their prevalence near transcription start sites and represent promising anticancer targets. Small molecules can bind to promoter G4s and stabilize the structure and may suppress oncogene transcription and inhibit downstream pathways. This work aimed to identify and validate G4 structures in the B-MYB promoter as potential therapeutic target. We demonstrated that the B-MYB promoter contains several G/C-rich motifs compatible with G4 formation. Using a combination of bioinformatics and biophysical techniques, we confirmed the existence of G4 structures in the promoter region. Additionally, we employed the G4access method to validate these G4 in a cellular context. Furthermore, we assessed the ability of G4 ligands to recognize and interact with the B-MYB G4, using spectroscopic techniques, and evaluated its biological outcomes. These findings highlight the potential of B-MYB G4 as a potential target for developing innovative cancer therapies.