Electroanalytical Biotools Targeting Globally Non-Canonical G-quadruplex DNA Structures: Towards Accessible Cancer Diagnosis and Therapy

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DNA research has moved beyond the classical double helix paradigm, uncovering the critical role of non-canonical secondary structures in essential biological processes such as replication, transcription, translation, and genome stability. Among these structures, G-quadruplexes (G4s) have emerged as dynamic "molecular switches," particularly enriched in genomic hotspots like telomeres and oncogene promoters, playing an active role in both cancer initiation and progression. Additionally, G4s influence transcriptome regulation, microRNA biogenesis, and both mutational and epigenetic landscapes. Their dysregulation has been reported across diverse biological matrices, including cultured cells, isolated chromosomes, tumor tissues, and even serum from colorectal cancer patients, highlighting their strong potential as biomarkers for accurate cancer diagnosis. Furthermore, the tunable stability and regulatory versatility of G4s make them highly promising targets for innovative therapeutic strategies in oncology [1-4]. Despite the increasing interest, current technologies for their visualization remain complex, expensive, and largely confined to highly specialized laboratories and personnel. These limitations pose a significant barrier to the widespread, inclusive, and effective detection of these structural motifs in clinical and biomedical settings. Therefore, as an innovative and still unexplored alternative, our research has focused on the development of the first electroanalytical biotool for the rapid, sensitive, and cost-effective detection of G4 structures at global level in DNA. In this communication, we will present the key principles of this innovative technology, which exhibits excellent sensitivity for G4 motifs quantification, detecting nM concentration in synthetic sequences and requiring as little as 50 ng of genomic DNA extracted from cancer cells. The bioplatform also exhibits high specificity, demonstrating the ability to discriminate between different synthetic G4 motifs within a characteristic fragment of the *c-Myc* oncogenic promoter –bearing distinct guanines substitutions that alter or render non-viable the G4 structure– as well as between cancer cell lines with distinct metastatic potential or gene-silencing profiles. This innovative approach offers a portable, affordable, and scalable solution to overcome current limitations in G4 quantification, enabling the rapid and reliable detection of gene-associated G4 markers at the point of need and paving the way for their integration into clinical practice, positioning it as a transformative tool for truly democratized and precise oncology.

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