

# Pioneering Electrochemical Peepholes for Decoding Epigenomic and Epitranscriptomic Oncological Landscapes

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The plastic, dynamic, and multilayered nature of life-threatening non-communicable diseases requires a multi-perspective clinical approach for effectively managing. Sadly, cancer remains one of the most prominent examples, in which single observations fail to capture its full biological complexity. To aid in this, diverse molecular biomarkers have been meticulously characterized at different omics layers, evolving from the well-standardized proteomics and genomics to the more intricate epigenomics and epitranscriptomics. However, the exploration of these mysterious omic strata is pointless if suitable technologies are not available to face this endeavor. Biosensing devices based on electrochemical signal transduction are continuously proving their limitless capabilities for accurate molecular markers testing, and their exploitation at the epigenomic and epitranscriptomic level is quite far from being an exception. In this communication, independent but closely connected recently developed electrochemical biosensing approaches for the multiplex detection of methylated adenosine (m6A) residues in microRNAs (miRNAs)<sup>[1]</sup> and the methylation–demethylation cycle – including 5-methyl-, 5-hydroxymethyl-, 5-formyl- and 5-carboxy- cytosines (5-mC, 5-hmC, 5-fC, and 5-caC)– in DNA at global level<sup>[2]</sup>, will be critically discussed. Both biosensing tools rely on the utilization of commercially available microparticles with magnetic properties as a solid base for their fabrication, biomolecular receptors, and HRP-conjugated tracers for the specific capture/label of the corresponding target epimarks, respectively, screen-printed tech-produced electrodes, and amperometry as signal detection modality. Praiseworthy analytical features exhibited by both biosensing approaches paved the ground for their practical implementation in the analysis of RNA and DNA fractions extracted from colorectal cancer (CRC)-derived cells and tumor tissues, in strong agreement with achieved results using alternative methodologies. Beyond their technical merits, these two implemented devices embody a remarkable pioneering contribution, as no electrochemical methods have been yet established for detecting miRNA methylation nor evaluating oxidative derivatives from DNA methylcytosine, thus evidencing their potential utility as reliable and operational diagnostic tools to elicit biological information at the epigenomic and epitranscriptomic scale, both holding valuable reserves about the evolution of oncological pathologies.

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## References

- [1] E. Povedano, V. Ruiz-Valdepeñas Montiel, R. Sebuyoya, et al. *Anal. Chem.* 96 (2024) 4580–4588.
- [2] E. Povedano, V. Pérez-Ginés, R. M. Torrente-Rodríguez, et al. *ACS. Sens.* 10 (2025) 2049–2059.