Dual electrochemical immunoplatform for the determination of epithelial glycoproteins associated with colorectal cancer aggressiveness

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Advances in cancer care and prevention include studying the role of candidate markers and the identification of new ones seeking the implementation of precision cancer medicine and minimal residual disease (MRD), to improve patients' survival, quality of life, and commitment to self-care and guarantee significant savings in healthcare costs. This progress depends to a great extent on the development of new disruptive technologies, including cutting-edge electrochemical bioplatforms, with the versatility of design and application required both to further explore the role of certain biomarkers and to identify new ones, and capable of meeting current pressing demands in terms of simplicity, reduced assay time, compatibility with multiplexed and/or multi-omics determinations, and applicability at the point-of-care (POC).

Mucin (MUC) proteins not only provide a suitable microenvironment to prevent hypoxia, acidity and other biological conditions that promote cancer progression, but also their composition and structure allows them to mimic the surface of normal epithelial cells, enabling tumour cells to escape immune surveillance [1]. The study of mucins' structure and function is an expanding field due to their clinical relevance, and their prospective use as potential therapeutic targets [2]. Among the mucin proteins family, transmembrane mucins 1 (MUC1 or CA15-3) and 16 (MUC16 or CA125) have been the most well-studied in terms of their clinical importance in tumorigenesis [3]. These two mucins are overexpressed in different types of cancer, including colorectal cancer (CRC), the second leading cause of cancer-related mortality worldwide, becoming particularly relevant in their progression [4].

In this work, the dual determination of MUC1 and MUC16 in extracts of CRC cells (1.0 µg per determination) with different metastatic potential is demonstrated. A disposable amperometric sandwich immunoplatform is used, it involving magnetic microsupports (MBs), a set of specific antibody pairs to intercalate each target protein (a capture antibody, cAb, and a biotinylated detector antibody b-dAb further labelled with a streptavidin-horseradish peroxidase, Strep-HRP, polymer), and amperometric detection on dual screen-printed carbon electrodes (SPdCEs) using the hydroquinone (HQ)/horseradish peroxidase (HRP)/H_2O_2 system. Under the optimised experimental conditions, this dual immunoplatform allows reaching limit of detection (LOD) values of 1.81 and 50 pg mL^{-1} (or mU mL^{-1}) for MUC16 and MUC1, respectively, and selectivity suitable for the determination of the two targets in clinical samples. These features together with its simplicity, multiplexing capacity, miniaturisation, and compatibility with POC devices, confirm that the developed bioplatform can be potentially employed to assist in both the early diagnosis of CRC and MRD detection, and demonstrates its competitiveness compared to ELISA and blotting technologies commonly used for the determination of these two mucins.

References

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