Available online at www.sciencedirect.com

ScienceDirect

Procedia Technology 27 (2017) 17 – 20

Procedia Technology

Biosensors 2016

Advanced electrochemical scaffolds for multiplexed biosensing of cancer reporters in complex clinical samples

Rebeca M. Torrente-Rodríguez[a], Susana Campuzano[a,*], Víctor Ruiz-Valdepeñas Montiel[a], Unai Eletxigerra[b], Josu Martinez-Perdiguero[c], Santos Merino[b], Rodrigo Barderas[d], Reynaldo Villalonga[a], José M. Pingarrón[a,*]

[a]*Departamento de Química Analítica, Facultad de CC. Químicas, Universidad Complutense de Madrid, E-28040 Madrid (Spain)*
[b]*Micro-NanoFabrication Unit, IK4-Tekniker, Eibar, Spain*
[c]*Departamento de Física de la Materia Condensada, Facultad de Ciencia y Tecnología, Universidad del Pais Vasco, 48080 Bilbao (Spain)*
[a]*Departamento de Bioquímica y Biología Molecular, Facultad de CC. Químicas, Universidad Complutense de Madrid, E-28040 Madrid (Spain)*

Abstract

Early and reliable diagnostic of cancer is mandatory to increase patient survival, thus requiring efficient and reliable analytical methods for such a purpose. Within this context, different strategies implying the development of electrochemical biosensors for the sensitive, selective and rapid multiplexed biosensing of genetic or protein cancer-related biomarkers are addressed in this presentation. In particular, novel sensing platforms have been developed for the determination of miRs, interleukin (IL)-8 mRNA, IL-8 protein, and cancer specific receptors. The developed methodologies allow for the determination of the target analytes at clinically relevant levels in complex samples: cancer cells, human tissues cell lysates, serum and raw saliva and can be easily extended to the determination of other relevant biomarkers.

Peer-review under responsibility of the organizing committee of Biosensors 2016

Keywords: multiplexed; electrochemical scaffolds; cancer biomarkers; clinical samples

1. Electrochemical biosensing scaffolds for multiplexed detection of cancer biomarkers

Cancer survival rates are generally low, due to a late and sometimes unreliable diagnosis of the disease that makes the treatment applied in certain cases not effective. Early detection is necessary to implement successful treatments, what can be achieved through information provided by various substances produced by cells, known as

Peer-review under responsibility of the organizing committee of Biosensors 2016
doi:10.1016/j.protcy.2017.04.010

biomarkers. These biomarkers, present in tumor tissues, serum and other biological fluids, comprise a wide variety of molecules including enzymes, glycoproteins, hormones, oncogenes and other related molecules [1].

Due to the heterogeneity of neoplastic diseases, detection of a single biomarker has limitations in controlling and predicting disease. Therefore, multiplex detection of several markers should lead to an early and more reliable cancer diagnosis, free of false positives [2,3]. Compared with traditional methods for cancer biomarkers detection, electrochemical biosensors are well recognized as promising candidates for the development of rapid, inexpensive, simple and highly sensitive and selective multiplexed miniaturized devices [4].

Within this context, relevant results achieved in the development of three novel biosensing platforms for the simultaneous interrogation of multiple biomarkers of the same and different nature and related to breast and oral cancer are briefly discussed herein. These multiplexed methodologies combine the well known advantages of disposable screen-printed electrodes with those of magnetic beads microcarriers (MBs) (Fig. 1). MBs have demonstrated to be attractive solid supports to carry out the recognition events which improved the performance of electrochemical biosensors in terms of sensitivity, reduced assay time and minimization of matrix effects [5,6]. Once modified with the corresponding bioconjugates, these particles are magnetically captured onto the surface of dual electrochemical transducers to perform the amperometric measurements, whose magnitudes are directly related to the concentration of the target biomarkers present in the sample.

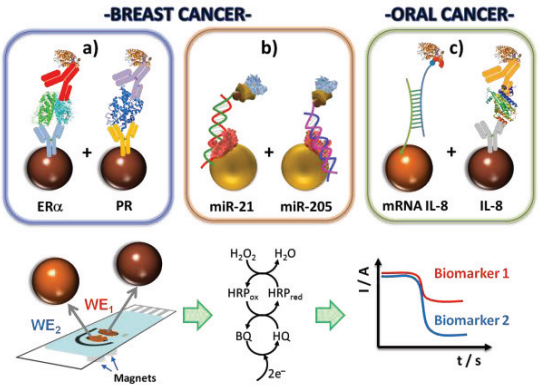

Fig. 1. Advanced electrochemical scaffolds developed for multiplexing cancer reporters.

1.1. Electrochemical bioplatforms for breast cancer diagnosis

Breast cancer (BC) is the most prevalent cancer and the second leading cause of cancer death in women, which makes prevention and control of this disease essential. BC is classified in 4 stages according to the size of the tumor and spread to lymph nodes and other parts of the body. In addition, according to the the expression level of estrogen (ER), progesterone (PR) and ErbB2 receptors, BC is classified as Luminal A, Luminal B, TNBC or ErbB2 subtype [7]. TNBC, with a considerable prevalence rate, is the most aggressive type of BC with no hormonal/ErbB2 therapies so that the developments of rapid and accurate methods for the detection of this BC subtype are highly important.

Progesterone and estrogens have been largely linked to breast cancer, and effective actions of these hormones imply the presence of ERα and PR in breast cells. These hormone receptors upon hormone binding produce signals that induce cancer cells to proliferate and grow. Testing for hormone receptors is important because the results help doctors decide whether the cancer is likely to respond to hormonal therapy or other treatments. A lack of any of these hormone receptors is associated with poor prognosis and usually indicates a decrease in a disease-free interval and survival. An amperometric magneto-actuated disposable immunosensing platform has been developed for the simultaneous detection of ERα and PR [8] by using two different batches of functionalized MBs bearing HRP-labeled sandwich immunocomplexes specific for each protein receptor (Fig. 1a). The usefulness of this dual immunosensing platform was demonstrated by analyzing raw lysates of two types of cancer cells with significantly different expression levels of both receptors. The obtained results, consistent with the differential expression of both