Biosensors and Bioelectronics 87 (2017) 285–298

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

New biorecognition molecules in biosensors for the detection of toxins

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ARTICLE INFO

Article history:
Received 20 April 2016
Received in revised form
17 June 2016
Accepted 28 June 2016

Keywords:
Bioreceptors
Novel designs
Biosensors
Toxin molecules
Future development

ABSTRACT

Biological and synthetic recognition elements are at the heart of the majority of modern bioreceptor assays. Traditionally, enzymes and antibodies have been integrated in the biosensor designs as a popular choice for the detection of toxin molecules. But since 1970s, alternative biological and synthetic binders have been emerged as a promising alternative to conventional biorecognition elements in detection systems for laboratory and field-based applications. Recent research has witnessed immense interest in the use of recombinant enzymatic methodologies and nanozymes to circumvent the drawbacks associated with natural enzymes. In the area of antibody production, technologies based on the modification of in vivo synthesized materials and in vitro approaches with development of "display "systems have been introduced in the recent years. Subsequently, molecularly-imprinted polymers and Peptide nucleic acid (PNAs) were developed as an attractive receptor with applications in the area of sample preparation and detection systems. In this article, we discuss all alternatives to conventional biomolecules employed in the detection of various toxin molecules We review recent developments in modified enzymes, nanozymes, nanobodies, aptamers, peptides, protein scaffolds and DNazymes. With the advent of nanostructures and new interface materials, these recognition elements will be major players in future biosensor development.

Contents

1. Introduction

A biosensor can be defined as a compact analytical device or unit incorporating a biological or biologically derived sensitive 'recognition' element integrated or associated with a physio-chemical transducer" (Turner, 2000). The bioreceptor recognizes the target analyte, while transducer converts the recognition event into a measurable signal. The uniqueness of a biosensor is that the two components are integrated into one single sensor (Fig. 1). This combination enables the measurement of target analyte without

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http://dx.doi.org/10.1016/j.bios.2016.06.083
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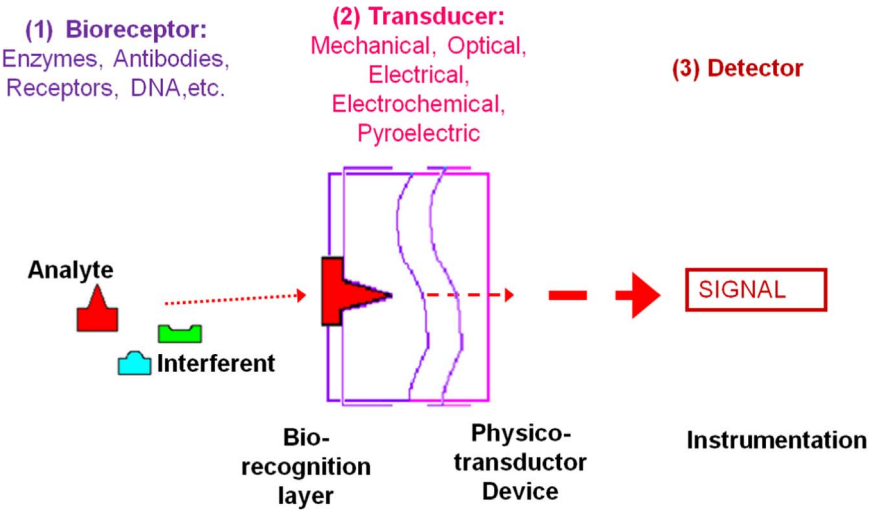

Fig. 1. Biosensor configuration showing biorecognition, interface, and transduction elements.

using extensive volume of reagents. For example, the glucose concentration in a blood sample can be measured directly by simply filing a mini drop of blood on the glucose biosensor. The main advantage of a biosensor is the simplicity and the quickness of measurements without requiring specialized laboratory skills.

In principle, any biomolecules and molecular assemblies that have the capability of recognizing a target analyte can be used as a bioreceptor. The first bio recognition element used in biosensor design was from living system. Depending on the nature of bioreceptor, catalytic or affinity biosensors were developed in the literature. Enzymes were the first recognition element integrated in biosensor designs with wide spread sensing applications. However, other bioreceptors molecules such as antibodies and protein affinity systems were introduced very shortly in the construct of biosensors.

Due to the emergence of bioengineering techniques, and the difficulties to obtain recognition element against small size molecules such as toxins or pollutants, many novel biosensor recognition elements have been developed and synthesized in laboratory.

2. Modified enzyme based recognition

Enzymes are the most widely used recognition element in the fabrication of various biosensors due to their specific binding affinities and catalytic activities. Recently, the catalytic enzymatic sensors have attained significant attention in biosensing applications due to their various measurable reaction products (light, electrons, protons and heat) arising from catalytic processes. Considering the needs of the reliable and robust sensing application, much effort has been done to design innovate and novel enzymatic sensor designs. To address the upcoming medical needs, researchers are interested to commercialize these sensors for the point of care testing. Among the developed enzyme based sensor, until now only the few methods have attained commercialized success such as glucose biosensors (Clark et al., 1962) and microfabricated electrophoresis chips (Chambers et al., 2008). However, the several disadvantages of enzyme sensor such as poor stability, critical operational condition, pH and temperature variation restrict their wider utility for real time applications. For example, the protein phosphates (PP1A and PP2A) are the enzymes which play a key role in various chemical reactions of cell physiology (Fig. 2). They are inhibited by a number of biotoxins (okadaic acid and its analogues, dinophysistoxins; DTX1, DTX2 and

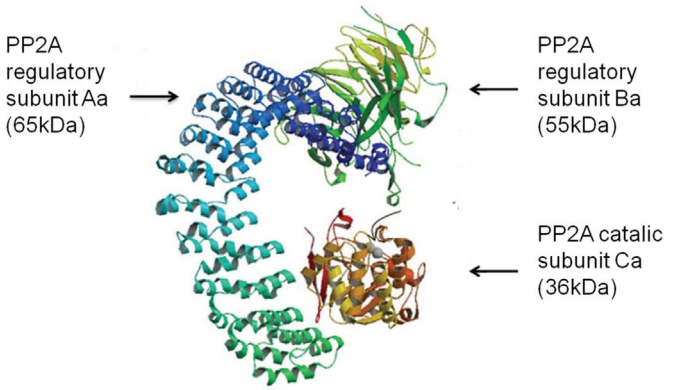

Fig. 2. Structure of PP2A. The quaternary protein structure is shown, composed of the catalytic subunit Cα, the 65 kDa regulatory subunit Aα, and the 55 kDa regulatory subunit Bα (Rubiolo et al., 2013).

DTX3) produced by marine algae and freshwater. The PP2A purified from animal tissues has limited applications due to lower enzyme activity and stability fluctuations. In thrust of improve stability, reliability, selective and sensitive measurements, scientific community explored the field of genetic engineering to develop the recombinant enzyme or to modify the catalytic/allosteric enzymatic sites. Various constructs of the PP2A inhibition-based biosensor have been reported for electrochemical monitoring of MC-LR in cyanobacterial cell samples (Campàs et al., 2005, 2007b) or for okadaic acid in marine samples (Volpe et al., 2009; Campàs and Marty, 2007c). In the same context, Rubiolo et al. (2013), genetically modified the PP2A catalytic site to enhance the enzyme stability and activity.

Acetylcholinesterase (AChEs), obtained from electric eel is used in 98% of the bioassay and biosensor designs for the detection of carbamates and organophosphates insecticides. The enzyme is considered very stable but lack of sensitivity against many insecticides restricts its applicability. To address this issue, Fournier (2005), produced hundreds of mutants of AChEs to improve the selectivity of enzyme towards the majority of the insecticides, and ability to discriminate in between insecticides such as organophosphate (OPs), carbamates and natural neurotoxic (anatoxin-a) (Villatte et al., 2002). Similarly, the functional expression of recombinant AChEs have been studied in rat, COC cells, baculovirus-insect cell system (Schulze et al., 2003). AChE-immobilized transducer surfaces have been used for detecting AChE inhibitors including organophosphorus and carbamate pesticides. The