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Recent advances in biosensor technology in assessment of early diabetes biomarkers

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ABSTRACT

Discovery of biosensors has acquired utmost importance in the field of healthcare. Recent advances in biological techniques and instrumentation involving nanomaterials, surface plasmon resonance, and aptasensors have developed innovative biosensors over classical methods. Integrated approaches provided a better perspective for developing specific and sensitive devices with wide potential applications. Type 2 diabetes mellitus is a complex disease affecting almost every tissue and organ system, with metabolic complications extending far beyond impaired glucose metabolism. Although there is no known cure for Type 2 diabetes, early diagnosis and interventions are critical to prevent this disease and can postpone or even prevent the serious complications that are associated with diabetes. Biomarkers for type 2 diabetes are useful for prediction and intervention of the disease at earlier stages. Proper selection of biomarkers that represent health and disease states is vital for disease diagnosis and treatment by detecting it before it manifests. In this respect, we provide an overview of different types of biosensors being used, ranging from electrochemical, fluorescence-based, nanomonitors, SPR-based, and field-effect transistor biosensors for early detection and management of diabetes with focus on prediabetes. In the future, novel non-invasive technologies combined with blood and tissue-based biomarkers will enable the detection, prevention, and treatment of diabetes and its complications long before overt disease develops.

1. Introduction

One of the most important healthcare challenges is the worldwide growing prevalence of type 2 diabetes (T2D). The disease is characterized by the insensitivity to insulin, known as insulin resistance (García-Jiménez et al., 2016). The etiology of insulin resistance is multi factorial and arises from numerous physiological stresses including genetics, physical inactivity, obesity, diet, medications, environmental toxicants, stress, and endocrine disturbances that all may result in disturbances of secretion of insulin (Khan et al., 2017; Hodjat et al., 2017; Johnson and Olefsky, 2013; Maqbool et al., 2016a; Mostafalou et al., 2012; Pakzad et al., 2013). The role of some famous environmental toxicants such as benzene (Bahadar et al., 2014a, 2015a, 2015b), xylene (Niaz et al., 2015), styren (Niaz et al., 2017a, 2017b), arsenic (Bahadar et al., 2014b; Khan et al., 2017), lead (Mostafalou et al., 2015), and mercury (Maqbool et al., 2014, 2016b, 2017) have been confirmed in the recent years. Many individuals with T2D are diagnosed after appearing several complications, which begin early in the progression from normal glucose tolerance to diabetes. The disease is a highly common disorder, as it directly impacts the quality of life of individuals. Diabetes health care spending accounts for more than billion dollars annually, including medical bills, medication, blood glucose assays, work loss and etc (Farshchi et al., 2014; Nichols et al., 2016). These observations indicate that early identification and management of individuals with a risk of T2D is necessary to reduce both the incidence of disease and its complications (Narayan et al., 2011;

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Hosseini and Abdollahi, 2013). Several studies have been conducted in the management of diabetes, such as administration of antioxidants (Rahimi et al., 2005; Tabatabaei-Malazy et al., 2013), development of new drugs, transplantation of isolated insulin producing cells, and clinical practice guidelines (Association, 2017; Tabatabaei-Malazy et al., 2016; Vakhshiteh et al., 2013). Multiple laboratory tests are used for the diagnosis and management of patients with T2D. The blood glucose concentration and HbA1c are the major diagnostic criteria for T2D and patient monitoring. It has long been known that more than 50 genes are involved in the performance of pancreatic β cell, insulin action, glucose metabolism, or any other circumstances that enhance the risk of T2D and these genes would be necessary to predict disease development. However, the outcome for candidate genes have been contradictory due to conflicting findings that probably related to small sample sizes, dissimilarities in T2D susceptibility across ethnic groups, differences in environmental exposures, and interactions between gene and environment. Hence, only few candidate genes were identified, including PPARγ, ABCC8, KCNJ11, and CALPN10 (Murea et al., 2012). The polygenic nature of T2D is complicated with loci affecting gluconeogenesis, glucose transport, and insulin homeostasis that lead to difficulties in predicting the incidence of diabetes. These limitations; however, can be overcome by considering multiple biomarkers for the prediction of T2D (Keating, 2015). The commonly available protein biomarker-based approaches utilized for the detection of T2D include enzyme-linked immunosorbent assay (ELISA), Western blot, enzyme immunoassay (EIA), and radioimmunoassy mass spectrometry. However, these techniques are burdened with a number of limitations such as availability, complexity, requiring modern infrastructure and equipment with skilled personnel, costly materials, and cost of time from testing to diagnosis (Cork et al., 2013; Parkash and Hanim Shueb, 2015). Biosensors can solve some of these problems. Biosensors are among the novel detection technologies in biomedical sciences defined as a single device platform that detects targets via biochemical reactions and transduces these reactions to electrical, thermal, or optical signals. These systems offer some advantages such as rapid detection, portability and patient flexibility (Hassani et al., 2016; Okafor et al., 2014). So far, the majority of designed biosensors for diabetes has focused on analysis of blood glucose and other biological fluids. In the current study, we have carried out an overview to identify biomarkers involved in impaired glucose tolerance and insulin resistance that results in prediabetes and ultimately T2D. Development of biosensors for early diagnosis of T2D would help to prevent or delay onset of the disease. Thus, we summarize the candidate biomarkers for early stage detection of prediabetes as well as the recent advances in development of biosensors for those biomarkers over the last decade. Eventually, we suggest critical biomarkers that have to be considered as potential targets for developing highly sensitive biosensors for T2D.

2. Biosensing technology

The classical approaches for analytical experiments, such as high performance liquid chromatography, GC, ELISA, or EIA offers quantitative data but qualitative. Moreover, extensive processing time, trained personnel requirements, as well as restriction in quantity of samples to be analyzed concurrently are regarded as additional negative points of old-fashioned methods. Hence, biosensor-based devices were introduced to advance presently detecting approaches, which offer several advantages such as high sensitivity and selectivity to its target, rapid processing period, friendliness, easy to implement, and being cost-beneficial. Biosensors have also improved processing steps and variability in signal transduction by incorporating biological and chemical sensing approaches (Kumar et al., 2015). Table 1 summarized a comparison between the characteristics of conventional methods and biosensing approaches.

Table 1
Comparison of traditional analytical and biosensing techniques.

Biosensor	**Pros**	**Cons**
	Fast real-time detection	Restricted commercial application
	Cost-effective	
	Transportable	
	Simple practice	
	High sensitivity	
	Controlled sample preparation	
	Reusable	
	Fewer organic solvent	
	Specificity	
Conventional analytical techniques	**Pros**	**Cons**
	Sensitivity	Long time procedure
		Costly
		Laboratory monitoring
		Skilled laboratory staff
		High-tech apparatus
	Specificity	Extended sample Preparation
		Not reusable
		Raised organic solvent
		Feeding

3. Classification of biosensors

3.1. Electrochemical biosensors

An electrochemical biosensor transforms the interaction between a biomolecule and target to an electric current or potential. Among several available biorecognition elements, enzymes are the major substrate owing to their specific binding ability as well as biocatalytic activity (Grieshaber et al., 2008). Various classifications have been introduced for electrochemical biosensors according to the signal property, which quantify the biological fluctuations in solution through potential, charge accumulation, current, conductance, or impedance. Generally, electrochemical biosensors have been categorized into amperometric, impedimetric, potentiometric, and conductometric biosensors. The sensitivity and selectivity of electrochemical biosensors principally linked to the biorecognition portion. The sensitivity is influenced by the conductivity of the materials as well. The transducer has an electrochemical feature which is thoroughly proportionate to the properties of electrode. Electrochemical biosensors are much suitable for miniaturization with well-matched sensitivity, simplicity, cost-effectiveness, and quickness.

3.2. Amperometric biosensors

Amperometric biosensors are among the most widespread types of biosensors, which principally quantify the current fluctuations prompted through an interaction between biosensor recognition element and the target, such as an enzyme or protein. The principle of amperometric biosensor for the target residue detection relies upon the potential or current caused by changes in the activity of recognition element before and after interaction with a target molecule (Grieshaber et al., 2008; Schuhmann, 1995). The remarkable advantage of this transducer is being low-priced as well as being very sensitive. In addition, application of disposable electrodes allows the system to exclude the requirement of repeated calibrations (Velasco-Garcia and Mottram, 2003).

3.3. Potentiometric biosensors

Basically, a potentiometer quantifies the changes in the potential variations in an electrochemical reaction generated across an ion-selective film separating two solutions at practically zero current flow.