Yeast-Based Biosensors

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Composed of a sensor part made up of live yeast cells coupled to a transducer/reporter technological element, yeast-based biosensors are powerful tools to detect and monitor environmental contaminants, toxins and generally organic or chemical markers of potential threat to human health. Yeasts are eukaryotic microorganisms very resistant to adverse environmental conditions but also able to sense and respond to a wide variety of stimuli. As eukaryotes, they constitute excellent cellular models to detect organic contaminants and chemicals harmful to animals. For these reasons, combined with their ease of culture and genetic modification, yeasts have often been chosen as biological elements of biosensors since the 1970s. Numerous different types of yeast-based biosensors have been developed for the environmental and medical domains, some of which are able to detect pathogens and viruses. The present technological developments of Synthesis Biology and Nanotechnologies further drive yeasts based biosensors into a new era where the biological element is optimized in a tailor-made fashion by *in silico* design and where the output signals can be recorded or followed on a smartphone.

Keywords: yeasts ; biosensors ; cell signaling ; environmental contaminants ; detection ; pathogens ; viruses

1. Introduction

Biosensors are among the most sensitive screening methods used to detect harmful chemicals and pollutants. According to their classically accepted definition, biosensors are composed of a biological recognition element able to sense or interact with the target molecules coupled to a physicochemical transducer and a microelectronic processor functioning as amplifiers and converters of the biological response into a measurable/numerical signal [1]. In these devices, the biological elements can be antibodies, specific proteins such as cell receptors or enzymes, nucleic acids, organelles, tissues, microorganisms, or whole cells. In this last category the whole cells, either eukaryotic or prokaryotic, are used as reporters with the advantage of combining both the biological receptor and the transducer elements in one [2]. Cells or micro-organisms used as whole-cell biosensors can be genetically modified in various ways in order to increase their sensitivity or to incorporate different reporter and transducer capacity [3][4].

2. Yeast-Based Biosensors

Most biosensors have been developed based on bacterial cells; however, eukaryotic cellular models present several relevant advantages. Among them, yeasts are of special interest, given their resistance to harsh environmental conditions, their successful long-term relationship with humans [5], and the fact that they are very well known at both technological and genetic levels. As eukaryotic organisms, yeasts share most cellular features and molecular mechanisms with our mammalian cells and notably several signaling pathways which are of great relevance towards sensing and responding to environmental stimuli. This high level of conservation has long driven scientists to use yeasts as model eukaryotes for the study of a wide range of cellular biology processes [6]. The best studied among yeasts species, *Saccharomyces cerevisiae* (also known as bakers' yeast) was the first eukaryotic organism whose genome was entirely sequenced [7] and is remarkably easy to modify genetically. Yeasts grow fast on inexpensive culture medium. They are very robust organisms that tolerate a wide range of temperatures, and they can be frozen or dehydrated for storage and transportation purposes. The combination of these elements (conservation of eukaryotic pathways and cellular mechanisms) with the practical aspects such as safety and easiness to cultivate, transport, and conserve yeast cells makes them an extremely interesting choice of biological model for the development of biosensors [5]. In addition, from an ethical point of view, the choice of yeast cells also allows using non-animal models to determine the potentially toxic effects of very diverse compounds or inversely to screen for therapeutic molecules (see below). Bioassays and biosensors based on yeast cells have been emerging over the years and are actually in use in various domains of application. The review [8] describes the different types of biosensors based on yeast cells with a special focus on environmental and medical applications; this distinction, however, is sometime hard to make and can appear arbitrary since what makes environmental contaminants harmful to Man or wild-life is precisely their effects on health. Hence some biosensors or yeast-based screens are relevant for both of these application domains.

Figure 1. depicts the general principle of yeast-based biosensors, with the possible inputs, the sensing and detection elements, and the desired output response.

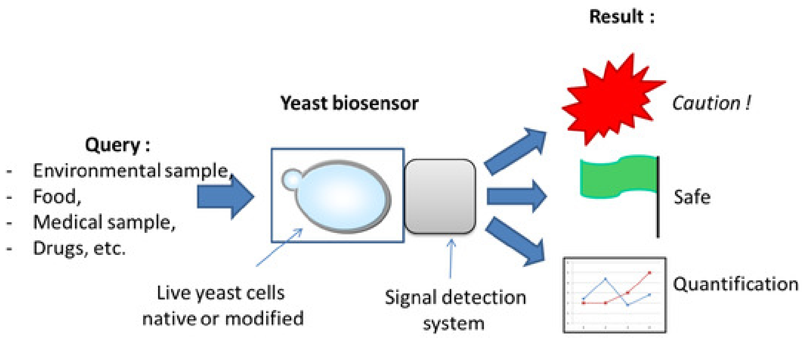

Figure 1. General scheme of a yeast biosensor's purpose and functioning. Different possible inputs appear on the left, in a non-exhaustive list. Live yeast cells are represented by a budding yeast shape inside of a supporting structure that is coupled to the signal detection system. Three main outputs are generally sought after by designers and users: either a "yes/no" answer in case a threshold level of the target molecule(s) exists, or a quantification value when needed and possible.

First, yeast cells either native or modified to constitutively produce luminescence can be used as non-specific reporter systems to monitor the toxicity toward eukaryotic cells of compounds found or used in food, the environment, building materials, cosmetology, drug design, etc. [9]. However, toxic compounds vary greatly in their cytotoxicity mechanisms; some are non-toxic for yeast cells while they may be toxic to human cells and tissues. In addition, yeasts have developed highly efficient detoxifications mechanisms and efflux pumps such as the pleiotropic drug resistance (PDR) family of ATP-binding cassette (ABC) transporters, which are able to export from the cell a broad range of chemically distinct molecules resulting in multidrug resistance [10].

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